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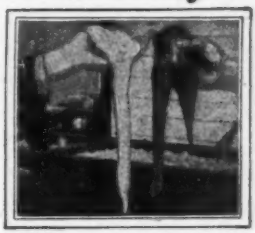

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MALTA FEVER IN THE UNITED STATES[1]

CHAS. W. WAINWRIGHT

From the Medical Clinic of the Johns Hopkins Hospital and University

For centuries there has loitered about the shores of the Mediterranean an obscure fever. Unobtrusive, it escaped detection until recently, hiding behind the infections that monopolized attention by the extent and gravity of their incursions. However, since the time of Hippocrates, shrewd clinicians have now and again noted unusual features that seemed to them to set apart this vagrant fever from the infesting hordes. The father of medicine himself records observations that lead us to believe the disease existed in his day. He describes protracted fevers lasting for many months, some with rhythmically recurring pyrexial waves that easily suggest the term undulant. We cannot prove that the disease thus pictured is the same as the one that now engages our attention, for it was only in 1859 that Marston gave the full and minute description which makes identification possible. This keen observer stationed at the Island of Malta had the opportunity to study many instances of a disease prevailing during the spring and summer, characterized by irregular relapses and remissions of fever, splenic enlargement, and a low mortality. He clearly distinguishes this disease from other febrile infections and particularly from typhoid fever, then prevalent upon this island, and by his careful clinical and pathological comparisons establishes a distinct nosological entity. Veale, in 1879, corroborates Marston's observations by giving an accurate account of the disease as it occurred in soldiers and sailors invalided from Malta to England, and differentiates it clearly from malarial fevers.

Bruce (2, 3, 4), in 1886, discovered in sections of the spleen of a patient dying of the disease, large numbers of bacteria. Later he was able to grow the organism from splenic pulp, and in 1891 isolated it from splenic blood, aspirated during life. Hughes (1) was able to

[1] This paper was read in part before the Southern Medical Association at Asheville, N. C., November 14, 1928.

cultivate the organism from cases of undulant fever during life and by inoculation into monkeys succeeded in producing a febrile condition ana ogous to undulant fever in man. Moreover, he recovered the organism from these animals and again produced the disease in others, thus establishing the etiology of the disease. He gave to the organism the name, *Micrococcus melitensis*. In 1897 Wright demonstrated specific agglutinins in the sera of patients suffering from the disease.

Because of the tremendous inroads made by the disease upon the personnel of the Army and Navy stationed at Malta, as well as upon the civilian population of the island, a commission, under the direction of Bruce, was appointed by the British Government (5), to investigate Mediterranean Fever. During the period from 1904 to 1907, most elaborate investigations were carried on concerning the isolation of the organism from patients suffering with the disease, and the life of the organism outside of the body. It was with some degree of surprise that it was discovered that the goat, used almost exclusively in Malta as a source of milk, not only was very susceptible to infection by melitensis but that a large percentage of the goats of apparently normal herds were infected. It was found that their sera gave positive agglutination reactions and that they were excreting organisms both in the urine and milk. About this time a herd of Maltese goats was brought to America on the steamship "Joshua Nicholson." The entire crew of the vessel, with the exception of a German cook developed Malta Fever. It was found that all of the crew had used raw milk from the herd except the German cook, who boiled all the milk he drank. When this herd was found to be infected and cases appeared in this country where milk from the same herd was used, it was demonstrated beyond question that the goat was the source of infection in human beings.

The discovery by Bang of the *Bacillus abortus* as the causative agent of contagious abortion in cattle was an event of equal importance in a seemingly entirely distinct field. This disease is prevalent in every part of the world where cattle are raised and has always been a serious economic problem. Evans, working in the Hygienic Laboratory in Washington, demonstrated the identity, or at least a very close similarity between the organism of contagious abortion and the organism of Malta Fever. They can be differentiated only by

agglutinin absorption tests. As early as 1913 Larson and Sedgwick (18) suggested the possibility of human infection with the abortus organism. However, it was not until the report of Keefer's (31) case, occurring in Baltimore, that it was proved that human infection with this organism occurred. It is now well established that the abortus variety of *Brucella melitensis* may infect human beings and produce a disease clinically indistinguishable from undulant fever of the Mediterranean. Four years later, Carpenter (38) isolated the organism from a patient's blood and also from the cow's milk consumed by the patient. Later, with these organisms, he produced abortion in pregnant heifers. Abortus disease in swine has been recognized for a number of years but it is only recently that we have realized how wide-spread it is. Reports of its occurrence have come from Kentucky, California, Missouri, Wisconsin and Illinois, and in certain human cases in which the infection could be traced to hogs the organism has been identified as the abortus strain. In France a number of cases not attributable to goats have occurred in slaughter-house workers and sheep have been suspected as the source of infection.

GEOGRAPHIC DISTRIBUTION

The first recognition of the disease was by the Medical Department of the British Army and Navy in Malta where it was seriously and regularly depleting the garrison. It was later seen along the shores of the Mediterranean, and soon made its appearance in Italy, Spain, France and Portugal. Gibraltar was almost as seriously affected as the base at Malta. Its occurrence in tropical Africa, in South Africa after the Boer War, in India, China and tropical Asia began to be reported. Musser and Cox saw the disease in Porto Rico, and Strong (12), Curry (11) and Chamberlin in the Philippines. Craig (6), in 1905, reported the first case observed in the United States. This case occurred in Washington, D. C., and was that of a nurse who had not been out of the country. It was impossible to trace the source of infection, but it was certainly not contracted from goats. Craig (7) later reports from Army Hospitals cases that originated in the Philippines, Porto Rico and Cuba. No other cases were reported in the United States until 1911, when Ferenbaugh, and Gentry and Ferenbaugh (13, 14, 15, 16) described cases occurring in Southwest

Texas. The following year Yount and Lourney (17) reported cases occurring in Arizona. In 1918 Woolsey (20) reported a case in Missouri, and in 1922 Lake described a number of cases occurring in Arizona among individuals using goats' milk. It was then realized that the disease had existed for at least twenty-five years in the Southwest United States, where goats brought from Malta had been raised. Keefer's report definitely established the possibility of human infection with the organism of infectious abortion and since his report instances of this disease have been cited in ever increasing numbers from all parts of the United States.

THE CAUSATIVE AGENT

Bruce worked with a coccoid form of the organism and described it as a micrococcus. In 1898 Durham described a bacillary form. The organism Bang described as the cause of contagious abortion is a bacillus. Evans (35), in her exhaustive work on the bacteriology of these organisms published in 1918, clarified the question of the morphology of Melitensis and demonstrated the intimate relationship between Melitensis and Abortus, showing that they were varieties of the same bacteriological species, and differed only in serological behavior. In 1920, Meyer and Shaw (22), proposed a new genus, the genus Brucella, in honor of the pioneer worker in the field. This classification is now generally adopted. Evans (35), working with some forty-nine strains of the organism from human, bovine, caprine, porcine and equine sources, was able to separate them by agglutinin absorption tests into seven serological groups:

Group I, designated Variety Abortus, contains chiefly bovine and porcine strains and two human strains.

Groups II and III, are most closely related. The former contains one bovine strain and the latter two human strains.

Group IV, designated Variety Melitensis A, contains eleven strains of human, bovine, equine and caprine origin.

Groups V, VI, VII, designated Variety Melitensis B, are predominantly coccoid forms.

The last three groups are doubtless the forms with which Bruce originally worked, and their coccoid form accounts for his original description of the organism as a micrococcus. These strains were

gathered from all parts of the world, and in addition to the above groups, there are certain Para Melitensis and Para Abortus groups of little importance in the practical consideration of the disease. It is Group I, Variety Abortus, and Group IV, Variety Melitensis A, that are of chief interest.

Evans' work has been confirmed by other investigators in Europe. Theobald Smith (32) however, feels that the identity of Variety Melitensis and Variety Abortus is open to question by reason of the definite hosts of the latter and the widespread occurrence of contagious abortion both in Europe and the United States. He also feels that the geographical distribution of Malta Fever, its relation to goats' milk and the apparently greater degree of infectiousness of Variety Melitensis militate against their identity.

Variety Melitensis and Variety Abortus are short, slender, pleomorphic rods with rounded ends, with practically identical average dimensions. They are readily stained with ordinary dyes but negative to Gram's stain. The first growth of Melitensis on agar usually required three days to make its appearance, while the initial growth of Abortus is often difficult to obtain. Various media and partial anaerobiosis have been tried without success. It is now recognized, as demonstrated by Huddleson and confirmed by Smith, that the organism grows best under increased CO_2 tension and appears in a shorter time. It is not safe to discard the cultures for at least two weeks unless such methods of culture are employed, and it is preferable that three weeks elapse before they are reported as negative. This applies most certainly to the bovine strains, while porcine strains apparently grow readily in air, and Francis even suggests that the ability of the organism to grow in air has possibilities as a method of differentiating the porcine strains from those of bovine origin. In Keefer's case the organism is reported as growing readily in air, and a further review of the history discloses that this patient was a laboratory Diener in the Department of Histology of the Johns Hopkins Medical School, and in such capacity was accustomed to make frequent trips to the abattoir to secure material for teaching. The material obtained was most frequently from swine, and it is altogether likely that the strain in this case was of porcine rather than bovine origin. The growth of the two varieties in broth is quite similar,

never becoming heavy and without a surface ring or pellicle. The sugars are not attacked by either variety but the pH of the media is reduced by both. Gelatin is not liquified and on potato the growth is glistening and brownish in color in both instances, but the coloring tends to become deeper in the case of Melitensis after several days have elapsed. This difference is, however, not striking and can not be considered a differential point.

With organisms so similar in their morphological, cultural, biochemical and serological characteristics, agglutinin absorption tests remain as the only differentiation available. By such procedure, however, the abortus variety can be distinguished without question from the melitensis variety. The classification of the various abortus strains offers an even more difficult problem. The ability to grow in air holds some promise as a method of differentiating the porcine strain as suggested by Francis. Theobald Smith (46) feels that the human strains can be identified when inoculated into guinea pigs by the polymorphonuclear invasion of the resulting lesion, and the suppurative infiltration with necrosis produced. He also describes similar lesions produced by porcine strains, while in lesions caused by bovine strains, necrosis never occurred. The primary reactions were identical in the three, and the differentiation became apparent only in the subsequent development. He feels, therefore, that porcine strains of the abortus variety are the source of human infection when Melitensis is not the causative agent.

Bassett-Smith (66) thinks that in countries where endemic abortion and infection of cows' milk are prevalent, undulant fever is rare, and that the abortus organism has a low power of infection for man. His conclusion is, therefore, that in America a double condition exists; abortus infection of cattle and hogs, and a secondary infection of cattle and hogs from goats, giving rise to the disease in this country. This opinion is open to question when one realizes that cattle raising is so universal in this country, while goat raising is carried on to such a limited extent and in only a relatively small area. McAlpin and Mickle report 90 per cent of the herds examined in Connecticut infected with abortus and only 60 per cent of the milk pasteurized. In over ten thousand blood sera examined routinely, only 63, or 0.6 per cent, showed a positive agglutination reaction in 1–100 dilution

or more. However, these examinations were not made in search of a cause for unexplained fevers. There seems to be no doubt that the abortus variety is less pathogenic for man than the melitensis variety. Smith reports the strain isolated from one of our cases as most like the bovine strains in its behavior in guinea pigs. This organism was recovered from the joints as well as from the blood stream of the case in question. A factor to be considered is the variation in the number of organisms in the milk, observed in goats by the British Commission and in cattle by observers in this country. Evans feels that climatic conditions may exert some effect upon the incidence of human infection in the United States. There is also the possibility that many cases are unrecognized, and this is a consideration which cannot be ignored.

CLINICAL PICTURE

Undulant fever presents a varied clinical picture. Its manifestations range from the mild ambulatory form, in which there are no or negligible symptoms to the malignant and frequently rapidly fatal form. Hughes described three distinct types; (*a*) *the intermittent type*, with insidious onset and mild course, and temperature rarely exceeding 100°F. to 101°. The symptoms are vague, the most prominent of which are headache, insomnia, anorexia and possibly epigastric tenderness, muscle or joint pains and sweats. The course is consistently mild and rarely do any more striking features present themselves. (*b*) *The undulant type*, the more common type, and in many respects the most typical of what the name 'undulant fever' implies. The undulant type of fever is more frequently seen, although here it may be distinctly intermittent with remissions and relapses. In this form the temperature elevations are higher, with headache, anorexia, insomnia, pains in the head, back and limbs, epigastric tenderness and obstinate constipation. Here, also, the profuse sweats so commonly seen occur with greatest frequency. (*c*) *The malignant type* occurs with sudden onset, runs a stormy course and is rapidly fatal. Fortunately it is by no means common, but does account for the greater part of the mortality rate of the disease. The fever reaches much higher proportions than in other forms and may even be extreme, with rapid development of the typhoid state, coma,

heart failure and death. (*d*) *The ambulatory type:* a fourth type which may be added, and a not inconsiderable number of cases fall into this group. Here there are few if any symptoms, and frequently the fever is so slight as to be unaccompanied by any discomfort. Cases of this type are often unrecognized unless sought for by an examination of the blood serum for specific agglutinins. The British Commission found many instances of this group during their investigations, and considered them possible carriers of a dangerous sort, by reason of the lack of visible evidence of their infection. Not only have organisms been recovered from the urine of such patients but the disease has been produced in monkeys and goats experimentally when inoculated with the urine of these patients.

With the disease occurring in such varied forms, it is not to be wondered at that recognition would in many instances be delayed or perhaps missed entirely, unless an epidemic was present or an obvious source of infection existed.

PREDISPOSING CAUSES

It was formerly thought that climatic conditions, bad sanitation, etc. were prominent predisposing causes. It is now generally accepted that there are no conditions predisposing to infection, and that infection depends only upon the entrance of virulent organisms in sufficient numbers into the body. This takes place by ingestion mainly, and less frequently by contacts of various sorts.

AGE INCIDENCE

The disease may occur at any age but is more prevalent during adult life. It is becoming more and more appreciated that it may occur among the young, and is recognized even in infants. While it is essentially a disease of young adult life, there is no reason why the young should be less affected then their elders.

INCUBATION PERIOD

This has been the subject of discussion since the disease was first recognized. The time necessary for the development of the disease has been given as varying from a few days to two or three weeks; and

numerous observers have cited series to prove this or that period of incubation. It was commonly felt, at the time of the first observations upon the disease, that the fever developed after quite long periods had elapsed, and many cases were cited in individuals after their return to England from Malta. Hughes felt, however, that in all of these cases investigated, the time could be reduced to at least fourteen days, and concluded that the usual period of incubation ranged from three to fifteen days. It was also the opinion of the British Commission that the average period of incubation was fourteen days. Craig, in this country, felt that the question was debatable and that cases developed after a period of incubation as long as twenty days. It is now generally agreed, such authorities as Bassett-Smith concurring, that the incubation period is about two weeks. As would be expected, however, laboratory and experimental infections occur in much shorter time, usually in from five to seven days. In such cases, it is to be presumed that the dose is probably overwhelming.

SYMPTOMS OF ONSET

The onset may be sudden and precipitous, when it is frequently ushered in with chilliness followed by high fever, sweats and severe headache, and the patient is acutely ill. This is seen in the malignant type, but is not the usual onset. On the contrary, there is a period of malaise, with general weakness, and usually the afternoon appearance of slight fever. The patient wonders what, if anything, is really wrong, but then observes that he fails to improve in a few days and the symptoms become more pronounced. The fever goes higher and he is compelled to submit. Headache, frequently frontal, occurs commonly at the onset and insomnia plays a prominent part. Often these symptoms are associated with aching joints or muscle groups and slight cough may be present. The symptoms are, however, ones that might be associated with the insidious onset of a number of acute infections and are in no way characteristic. There is usually anorexia, a coated tongue, and at times more or less nausea or even vomiting, the last being present in the more acute cases. Constipation is described as present from onset, but it is most commonly a later development. Diarrhea also has been observed but is even

more infrequent. Other symptoms which occasionally make their appearance at the outset are abdominal tenderness (epigastric), weakness, nervousness and irritability. Unless the initial symptoms are severe, one usually discounts them until he realizes that what at first seemed trifling is attaining the proportions of a serious illness. Should the infection be ambulant or of the mild type, he is in most instances entirely unaware of the nature of his illness, or it passes after several days unrecognized, and he or the world is none the wiser.

The course of the more unfortunate ones is not infrequently long drawn out, and when fever, chills and sweats, the triad commonly present in the disease, make their appearance, the infection should at least be suspected. The usual course of events is for these features to subside after from fourteen days to six weeks and a remission of varying length to occur. A relapse ensues, and with its appearance the condition is clinically recognized. The relapse is not uncommonly experienced a number of times, and even one or two would be as discouraging as they are in typhoid fever. When six or eight or ten follow, however, one's morale is rapidly shattered and there seems no hope. While one attack may terminate the infection, the remission and relapse coming repeatedly is the rule and any number of relapses may be experienced.

The symptoms of onset increase in severity as the disease progresses. The temperature mounts higher on each succeeding day usually with morning remissions, although it may be continuous in type, and nervous symptoms become pronounced. It is not extraordinary to see the temperature reach 104° or 105° in the afternoon. The wavy character of the fever during the course of an attack has been described as characteristic, but it would seem that more importance has been attached to this feature than it warrants. One gets the impression that the temperature may be of any type, and is, in fact, more frequently irregular than conforming to any particular type. Hughes described all types of temperature, and Craig felt that the temperature curve was in no way characteristic. These symptoms are not infrequently augmented by chilly sensations, rarely true rigors, and the severe sweats, so frequently described as "drenching," are seen at this stage. The patient frequently cannot sleep, is restless and irritable, and headache—frontal or occipital or both—is

severe. The headache is in many instances proportional to the amount of fever and, in fact, the intensity of all the symptoms varies with the degree of fever. The patient complains of pains all over, especially in the back and neck, and these are often exaggerated by motion. The insomnia is not uncommonly an early symptom but the sufferers are clear mentally and delirium rarely appears except in severe cases. Neuritic pains are commonly late occurrences, and are even described as sequelae, but occur in a large proportion of cases. Once they make their appearance, they persist frequently for long periods of time, resistent to any type of therapy.

The joint symptoms, usually vague at onset, develop with the establishment of the infection and are often acute. Effusion into the joint is often present, as well as swelling, tenderness and severe pain. Suppuration apparently never occurs, although in a number of instances the organisms have been recovered from the joints. Practically all the joints are involved, but the hips, knees, shoulders, ankles, wrists and fingers are most frequently affected. The duration of these acute features is from a few hours to a few days. The joint manifestations are at times chronic in nature and chronic articular rheumatism is a not infrequent diagnosis. Craig, and later Curry, was much impressed with the frequency of this diagnosis. Their observations were made in the Government Hospital at Hot Springs, Arkansas, where many patients with a diagnosis of chronic rheumatism, which was resistent to any and all types of therapy, were seen.

In other instances actual bone change takes place, Cignozzi (26) reports two cases considered tuberculosis of the hip joint. There was in these cases a decided tendency to heal, which would arouse one's suspicion, and recovery did actually take place in from two to three months. The bone change occurring in Malta Fever, while apparently not frequent, is, nevertheless, definite, and can be distinguished from tuberculosis. In tuberculosis of a joint the change, as demonstrated by X-ray, takes place in the articulating surface. In Malta fever this is never involved, but there is absorption behind the articulation. Such a case, clinically Pott's Disease, has recently come to our attention in which there was a complete recovery.

The respiratory symptoms never occupy a prominent place, except in the few cases in which bronchitis and occasionally broncho-

pneumonia are complications. One frequently sees, however, some congestion of the bases of the lungs. In broncho-pneumonia, when present, there is nothing characteristic and it is similar to that seen often in the course of many acute febrile illnesses. It is at times a terminal event.

Anorexia is the first of the gastro-intestinal manifestations to appear and is very frequently an initial symptom. It may be accompanied by nausea and even vomiting. The latter is rare but is seen in some of the more severe cases. Epigastric tenderness is quite common, and pain in the region of the liver or spleen, or both, is frequently present. In many cases both organs are enlarged as well as tender. Constipation is the outstanding gastro-intestinal symptom and is commonly described as protracted and severe. Diarrhea, while occasionally seen, is rare and usually gives way to severe constipation.

Orchitis and epididymitis occur in a small percentage of cases and oöphoritis is also seen. These manifestations are infrequent, usually not severe, and suppuration is not seen; nor is there any diminution in sexual function as a result of these complications.

PHYSICAL FINDINGS

A striking feature of the disease is the small number of objective findings. Not infrequently one sees a patient who is acutely ill with high fever and prostration, and the physical examination yields nothing. Perhaps the most constant findings are in the abdomen, where epigastric tenderness can be elicited or tenderness in the region of the spleen, associated with splenic enlargement. Increase in the size of the spleen is considered a very characteristic feature of the disease. Hepatic enlargement may be present, and at times hepatic tenderness is found. The abdomen yields nothing, beyond this, unless there is some measure of tympanites accompanying the constipation, so frequently present. Cough, with signs of basal congestion, is now and again seen, but in these there is nothing distinctive. When there are joint manifestations present any of the joints may be tender on handling and on motion, with swelling and increase in local heat but rarely, if ever, any redness. Effusion into the joints occurs and when present is obvious but never goes on to suppuration.

At times there is rather severe instability of the nervous system

with exaggerated reflexes, occasional clonus, and at times even evidences of meningeal irritation.

While glandular enlargements have been described, these are quite infrequent, and apparently have no association with the disease.

Of course, if the illness is of long duration, there are the evidences of any protracted febrile illness,—loss of weight, anemia, etc., but these are found only in such instances and are not a part of the initial picture.

While the disease is a septicemia, aside from the joints, focal manifestations are uncommon. In a small number of cases orchitis and oöphoritis occur, but suppuration rarely, if ever, takes place and in these focal lesions no destruction is evident. Eyre (9), however, has reported an instance of hepatic and subphrenic abscess from which only Melitensis was obtained, but this is certainly the exception rather than the rule.

LABORATORY EXAMINATIONS

It is commonly said that undulant fever is associated with a severe secondary anemia, which is quite true in protracted cases and after relapses have occurred. In the initial stages, however, unless there is anemia from some other cause, it is not found. The erythrocytes, on the contrary, appear quite normal and their hemoglobin content is within normal limits. After the disease has been present for an extensive period, anemia, often a severe grade, develops, as would occur in any long continued illness. It is not uncommon in these instances to see hemoglobin determinations below 50 per cent with correspondingly reduced red cell counts.

The white blood cells very frequently, in fact as a rule, show marked variations from the normal both in the actual number present and in the differential formula. On the other hand, pathological white blood cells are not seen. Craig (7) observed in a number of his cases a leucocytosis, and felt that this was an important differential point in distinguishing the disease from typhoid fever. While moderate leucocytosis has since been observed,—Keefer found such in his case—the common observation is a leucopenia, not infrequently as low as 3,000. In some instances, a normal white cell count is found. The usual finding in the differential formula is a lowered polymorpho-

nuclear percentage. This type of cell is decreased to as low as 40 per cent, and not infrequently to 30 per cent of the total number present, with a corresponding increase in mononuclear cells. This increase is usually seen in the total lymphocytes, the percentage being as much as 60 or even 70 per cent, while less frequently the mononuclear-transitional group shows a definite increase.

The organism is searched for in the blood and it is in blood culture, together with agglutination reactions, that the diagnosis is confirmed and in the large majority of cases made. The British Commission found the organism in the blood in considerably over half of a series of 150 cases. It was observed that there was no relation between the stage of the infection and the presence of the organism in the blood, as it was found as early as the second day and as late as the three-hundredth day of the disease. It has also been isolated after the temperature has been normal for several days. Keefer was able to recover it from his case several weeks after the fever and symptoms had disappeared. Some diurnal variation has been found, positive cultures being more readily obtained in the evening.

The urine shows no abnormality save albuminuria which is so frequently observed in any febrile illness. The organism is, however, excreted in the urine of human beings as well as infected animals. The British Commission found Melitensis present in the urine in about 50 per cent of their cases, but this is considerably more than its recovery in this country in either the Melitensis or Abortus infections seen. They also observed that it tended to be excreted either in a sudden gush, stopping as quickly as it appeared, or in small numbers over a long period of time. Recovery from the urine is more likely as a wave of fever is subsiding, and the excretion tends to cease with the onset of a relapse. It is quite rare that the organism is cultured from the urine if it has not been obtained from the blood, although such cases are reported.

AGGLUTINATION TEST

On this procedure, in a large majority of instances, the diagnosis of Malta Fever depends. The importance of Wright's observation was far reaching. It doubtless would have been observed in due course of time, but it added materially to the detection of infections

in so many of which bacteremia could not be demonstrated. The agglutination reaction is of infinite value also in tracing the source of infection, having been demonstrated not only in the sera of goats and cattle but also in the milk of these animals, and in the sera of swine and the other less frequent sources of infection. The reaction is obtained with either variety of the organism in practically equal dilutions, and is specific, except in one instance. Evans (40) observed that about one-third of a series of 100 cases of tularaemia showed cross agglutination with abortus and melitensis. In but three instances of this series there was a distinct difference in the titre to such an extent that the sera could be classified by the higher titre. In the cases in which the titre is the same, and the diagnosis not otherwise obvious, the serum should be subjected to agglutinin absorption tests. Francis has made similar observations, and confirmed entirely Evans' work.

The degree of agglutination is a matter of considerable importance. The British Commission found that there was apparently no relation between the agglutinating power of the serum and the degree of the blood stream infection. In most cases it was found high when organisms were present in the blood stream. However, this is not always the case. Carpenter (38) reports a series of five patients in which agglutinins were present in but three, whereas the organism was obtained from the blood in all. Kennedy reports a case in which there was no serum reaction in a dilution of 1–40, but the organism was obtained from fluid withdrawn from the subdeltoid bursa. In addition to these there are a number of instances of extremely low titre in the presence of a blood stream infection. Bassett-Smith feels that in chronic cachectic cases the reaction is often difficult to obtain and is obtainable in only low dilutions. In one of Carpenter's cases both typhoid bacillus and bacillus abortus were recovered from the blood, and the patient's serum agglutinated typhoid 1–60, but failed to agglutinate abortus. The British Commission found no cases of Malta Fever and Typhoid Fever existing concurrently, but found a number of cases in which typhoid followed Malta Fever. Fici (29) reports positive reactions in 10 of 98 cases of tuberculosis but concludes that tuberculous sera show no specific property toward Melitensis, and this view is corroborated by Giordano and Ableson (77)

in this country. There are also instances in the literature of non-specific reactions with melitensis and abortus in normal sera from febrile cases, but these will disappear when the serum is heated to 56° for thirty minutes. It is not known, however, what effect other infections have upon the production of agglutinins in Malta Fever, whether multiple agglutinins are produced, or the normal development is influenced by concurrent infection. Carpenter points out the fact that certain strains of both melitensis and abortus make better antigen than others, which may be a factor in the instances of absent titre. It has been demonstrated, beyond question, that the agglutination reaction cannot always be relied upon to make the diagnosis. If there is a blood stream infection when the reaction is absent, all well and good, but one sees cases in the absence of both blood stream infection and agglutination reaction in which the disease is clinically Malta Fever without doubt.

What titre then is conclusive evidence of infection? Evans feels that the reaction in dilutions of 1–40 and higher is conclusive evidence of the disease past or present, while Bassett-Smith is willing to accept, as evidence of infection, dilutions of 1–30 and feels that lower dilutions are suspicious. It is important, however, that the test be made in all practical dilutions, as a proagglutinoid zone, as occurred in Keefer's case, can occur. Evans (76), in her work, has never seen the proagglutinoid zone, which may be due to the method she uses in performing the test, but it is a well recognized, though little understood, phenomenon and can occur. It, also, was found by the British Commission that at times certain dilutions were skipped in the reaction, a phenomenon observed in Baker's case of intermittent hydrathrosis, but not reported because it could not be confirmed. One attack apparently confers an immunity to the disease but the titre is apt rapidly to diminish and in time disappear.

DERMAL REACTIONS

Burnet (70) has reported positive reactions with intracutaneous injections of Berkefeld filtrate of broth cultures of variety Melitensis. Giordano and Ableson (77) have studied vaccines made from an abortus strain obtained from one of their cases but reports less promising results from filtrates. Trenti found the intracutaneous reaction

valuable in diagnosis but it did not entirely parallel the agglutination test. The test is neither standardized nor sufficiently observed to warrant any conclusions.

It is apparent then that there is no disease in which the diagnosis is more dependent upon laboratory procedures than is Malta Fever. We do blood cultures and Widal reactions in continued and unexplained fevers as a matter of routine. It is extremely important that Malta Fever be kept in mind in all continued or recurrent fevers, and that agglutination tests be done to rule out this infection. The disease is one in which the clinical manifestations may be so much at variance with the usual picture as to lead one completely astray. In the interpretation of the agglutination test it must be borne in mind that negative results do not eliminate the disease from consideration.

PATHOLOGY

The pathological anatomy of Malta Fever, because of its low mortality, about 2 per cent, has been but little studied. The British Commission was able to recover variety Melitensis from the spleen and liver post mortem in 100 per cent of their examinations. They obtained it frequently from the mesenteric and femoral lymph glands and heart's blood, and occasionally from the pericardial fluid, bone marrow and bile. Bruce and Hughes not only recovered the organism from the spleen by culture, but record any number of observations of the organism in large numbers in sections of the spleen, and occasionally in sections of the liver and kidneys. Carpenter has isolated the abortus variety from the tonsils. Giordano and Ableson (77) suggest this, together with the degree of involvement of spleen and liver in experimental animals, and the occurrence of gall bladder infection, in one of their cases, as possible evidence of foci in which the organisms are harbored for long periods of time. In one of the cases of our series, to be later considered, the organism was recovered in pure culture from an ovarian cyst six years after the initial symptoms. These focal manifestations cannot be passed without consideration. Certainly the long duration of the illnesses suggests most strongly that unrecognized foci exist, and this feature of the disease needs more study.

The only observations upon autopsy material available are those made by Hughes in his investigations of the disease. One is impressed by the lack of anything distinctive in these descriptions, and would conclude rather that it is largely postmortem change that he describes. It is difficult to evaluate his findings in the spleen. The enlargement and softening of the organ are typical of the acute splenic tumor one would expect to find in any infection. He describes as most characteristic a broken down appearance of the spleen in acute cases in which the organism has the appearance of a large clot of blood. It is difficult, however, to understand just what this change represents.

The lymphoid tissue of the intestine is uninvolved as is the lymphoid tissue of the body generally, but both Bruce and Hughes record instances in which the mesenteric glands are enlarged.

The pathological reports since these observations were made have been meagre, and only from time to time have cases been reported. In these cases an increase in the size of the spleen is reported, with marked increase in the fibrous elements, and no increase of the splenic pulp. Scott and Shopher (72) report a case of acute endocarditis superimposed upon an old rheumatic endocarditis, but to what extent Malta Fever is responsible for the added acute lesion is not clear. In this case there was splenic hyperplasia. In some instances the organism has been recovered from the spleen post mortem. The only instance of actual suppuration recorded is that reported by Eyre, mentioned above, in which Melitensis was the only organism recovered from the abscesses present.

TREATMENT

The disease is fast attaining the proportions of a public health problem and means of prevention, therefore, take a prominent place. This is particularly true because of the absence of any specific remedy and the apparent futility of any of the present methods of attack. It is not the mortality rate but the prolonged debilitating effect that gives the disease its importance as a public health problem. We are now meeting the problem of bovine tuberculosis in an intelligent manner and until we are able similarly to approach Malta Fever it will continue to spread. It is true that pasteurization renders the milk usable, as both varieties of the organism are killed by the process.

In the rural sections such a procedure is not only impractical, but well nigh impossible, for who, accustomed to drinking raw milk, will ever consent to its pasteurization? Such a case has recently come under our observation; the brother of a patient, in whom the diagnosis has been made and the source of infection traced to a cow used as a milk supply, became ill with the disease. Pasteurization of the milk had been advised after the first diagnosis had been made but was soon discontinued, with the resulting spread of infection.

Wright, in 1895, attempted to produce an antiserum by treating a horse and later goats by subcutaneous injection of killed cultures. The serum was of little value either as a curative or a protective measure and possessed but little agglutinative power. Further experiments by members of the British Commission demonstrated that there was little relationship between the agglutinins present and any antitoxic or antibacterial substances created, and the blood of infected experimental animals frequently showed a high titre for some time prior to death. There was generally present, however, in those animals with a low titre a blood stream infection, while it was in most instances absent or not demonstrable in those with a high titre. In their attempts with vaccines it was observed that injection of killed cultures tended to cause an immediate diminution and later an increase in the titre. If, however, the injections were made too frequently the diminution was cumulative. After developing a high titre in rabbits the animals were invariably killed by small injections of living cultures, and the sera of these treated animals failed to protect normal rabbits or modify the course of an infection.

Bassett-Smith (25) feels that there is benefit to be derived from the use of vaccine. He cites sixty-one cases treated with a stock vaccine, in which an initial slightly negative phase in the opsonic index was changed to a sustained high positive one, without constitutional disturbances and without abscess formation at the site of inoculation. (In one of our cases treated with vaccine we regularly produced sterile abscesses at the site of inoculation in spite of every measure to prevent it.) He feels, however, that vaccine is of no value during the acute stages, whereas in the chronic cases with slight fever there is benefit to be derived, and in some cases vaccine given on a rising wave of fever has altered the course.

Nicolli and Conseil (30) report protection in humans by subcutaneous injection of vaccine against subsequent injection of living organisms, and De Finis (28), likewise, favorable results in fifty-five cases of Malta Fever treated by use of vaccine.

Many have turned to chemo-therapeutic measures in an effort to combat the disease, using mercurochrome intravenously, and the literature contains numerous instances of such therapy. Many of these records are meagre, however, and merely report recovery after one or two injections have been made. Ross and Martin (57) report nine cases in Rhodesia treated by intravenous mercurochrome injections. In five of these cases the organism had been obtained from the blood stream. In three cases there was improvement, one prompt and two gradual. In the remaining six cases no improvement was obtained after five to nine weeks' observation. There are other reports of more satisfactory results after its use, but Ross and Martin concluded from their experiments *in vitro* that the drug had no direct effect upon melitensis or abortus in concentrations possible to be obtained in the blood stream, and it possessed no definite value as a method of therapy. We understand that those most active in the investigation of the clinical applications of the drug agree with their conclusion as to its mode of action, and it is their feeling that its action is not due to any direct bactericidal effect. They do feel, however, that it has therapeutic value and that cures are obtained by its use.

REVIEW OF THE AMERICAN CASES

The American occurrence of the disease begins with the report of Craig's first case, a nurse in Washington, D. C., in 1905. We do not know whether this infection was caused by variety melitensis or variety abortus, but only that clinically it was Undulant Fever, substantiated by positive agglutination reactions. No history of contact with goats or the use of goat's milk could be obtained. In addition to this case, he reports several cases seen in the Army hospitals, imported from the Philippines and West Indies. Musser, Curry and others have described similar imported cases. This Huddleson (67) describes as the first period in the history of the disease in the United States. He further separates as the second

period the identification of the disease in the Southwest, where it had been endemic for a number of years. Here infected goats imported from Europe were responsible for the occurrence of the disease, and the infection was undoubtedly due to variety melitensis. A disease, known as "goat fever," had been present in Texas and southwest United States since before the beginning of the century, but was not recognized as Malta Fever. In 1911, Ferenbaugh, and later Gentry and Ferenbaugh describe a series of twelve cases in Texas in individuals either using unboiled goats' milk or actively connected with goat raising and establish this infection as Malta Fever. The third period concerns the present time, beginning with the report of Keefer's case in 1924, when abortus infection in man was first established. Since that date in all parts of the country infection with variety abortus has been described, and an ever increasing literature is accumulating. In going over the literature of the American occurrence of the disease we have gathered 74 cases of definite Malta Fever occurring in the United States, in which the record was in any measure complete. To this number we have been able to add 8 cases, four seen at the Johns Hopkins Hospital, and four seen in private practice, making a total of 82 cases. We were able to classify 51 of these cases as instances of abortus infection, while 25 were instances of melitensis infection. In 6 it was entirely impossible to make a distinction. In by no means all of these cases was the variety of the organism causing the infection definitely established. By reason of the history, the geographical distribution, etc., in those in which the variety was not proved, it seemed sufficiently definite to make the distinction. From Fig. 1 it is readily seen that with the exception of one case in Missouri the instances of melitensis infection have occurred in the Southwest where the goat raising is carried on and where goats' milk is used extensively. The instances of abortus infection, on the other hand, are in the eastern half of the United States and largely in the states where cattle are raised. With each succeeding year the number of cases appearing in the literature increases as the disease is more generally recognized and examinations of the blood made to detect its presence. In order to determine more accurately the occurrence and distribution of the disease, we have obtained from the Boards of Health of forty states and the District of Columbia and

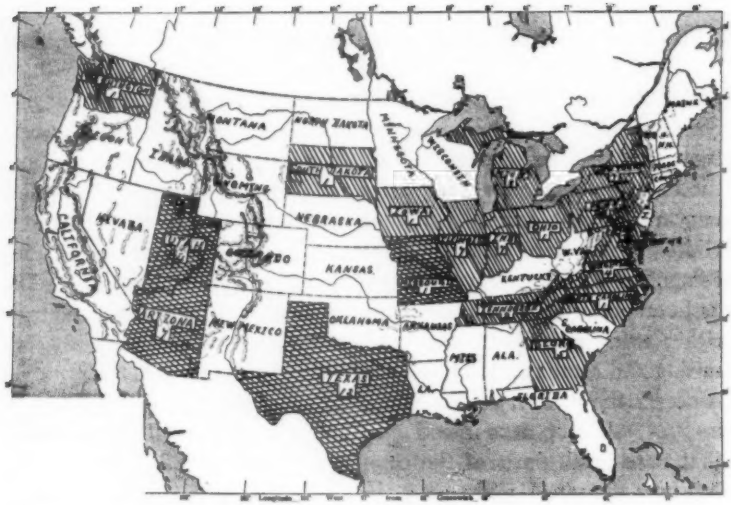

FIG. 1. DISTRIBUTION OF CASES OF MALTA FEVER IN THE UNITED STATES, REPORTED IN THE LITERATURE

The states with crossed lines are those in which Melitensis infections occurred, and the states with straight lines those in which Abortus infection occurred.

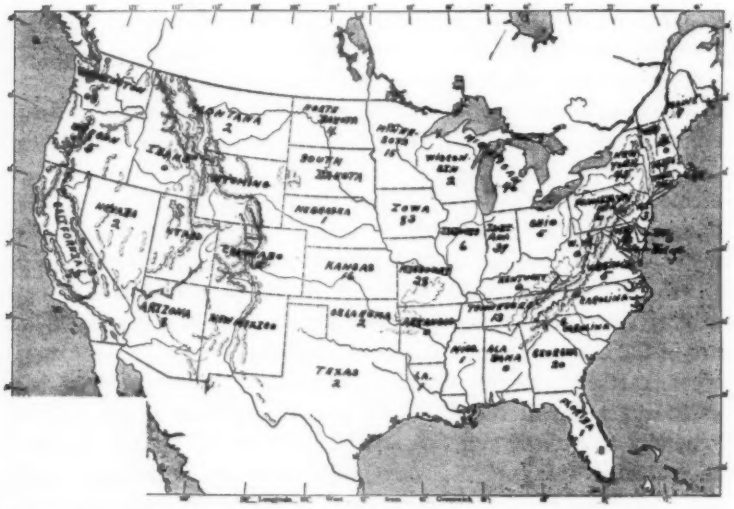

FIG. 2. DISTRIBUTION OF THE CASES OF MALTA FEVER IN THE UNITED STATES REPORTED TO THE BOARDS OF HEALTH OF 40 STATES AND THE DISTRICT OF COLUMBIA, FROM JANUARY 1, 1927 TO JULY 1, 1928

from the United States Public Health Service 422 instances of the disease occurring in the eighteen months period from January 1, 1927, to July 1, 1928. The distribution of these cases is seen in Fig. 2. Even this does not give us a fair estimate of the occurrence of the disease, as in a number of states the disease was not made reportable until July, 1928. Five cases are reported in Ohio during the eighteen months period above referred to, whereas twenty-one cases have been reported from July to October, 1928. In Missouri, thirty-two cases are reported in the three months subsequent to July 1, 1928, and only twenty-eight cases in the eighteen months preceding. We see that the disease is rather generally distributed throughout the country, but the greater number of cases tends to be in the dairying states, and from those sections in which we find most of the instances of abortus infection in the literature. We feel that this survey by no means pictures the actual prevalence of the disease, but does show that it is vastly more common than the reports in the literature would lead one to believe.

Kern (78) has recently published a review of the reported cases of abortus infection occurring in the United States, citing some thirty-six cases, and many of his cases are included in this group. We have been able, however, to supplement his series, and certain comparative considerations brought out in reviewing the instances of melitensis infection with those of abortus infection we feel are worthy of comment.

CLINICAL CONSIDERATIONS

Age incidence. Both infections occurred in all decades from the first to the sixth, while one instance of abortus infection occurred in the seventh decade. (See Chart I.) It will be seen that the majority of cases in both infections occurred in the third, fourth and fifth decades. The occurrence of five instances of abortus infection in the first decade we feel is of significance. Does this mean that there is a likelihood that the group of unexplained fevers in infants contains more instances of abortus infection than we realize? Larson and Sedgewick found that 72 children in a group of 425 gave positive agglutinations. They concluded that these reactions indicated a positive immunity, the result of receiving the organisms in ingested

milk, whether any symptoms were detected or not, and did not represent a passive immunity due to the absorption of antibodies from the milk. While the reports of cases in the first decade are few it would certainly seem reasonable that infection would occur at the time of life when milk was such a large part of the diet.

Sex. It is not reasonable to conclude from these figures (Chart II) that males consume more milk than females, but that other means of infection than by ingestion exist. The more intimate contact of males with infected animals at once offers itself as an explanation and it seems altogether likely that this is the cause.

	FIRST DECADE	SECOND DECADE	THIRD DECADE	FOURTH DECADE	FIFTH DECADE	SIXTH DECADE	SEVENTH DECADE
Melitensis	2	6	7	3	3	2	
Abortus	5	5	10	10	9	4	1

CHART I. AGE INCIDENCE

	MALES		FEMALES	
	Cases	Per cent	Cases	Per cent
Melitensis	20	80	4	16
Abortus	33	65	10	22

CHART II. SEX

Occupation. In the melitensis infections 15 were goat raisers and herders working with goats and using raw goat's milk; one a veterinarian, one a bacteriologist, one a school-girl, and one a soda fountain clerk, while in five instances there was no record of the occupation.

In the abortus group five were in children under six years of age, six were bacteriologists, four farmers, two farmers' wives, three physicians, two electricians, two students, two laboratory helpers, one a farm machine demonstrator, one a butter maker, one a nurse and one a clerk. In eight cases no occupation was recorded.

Practically all of the melitensis infections were among those engaged

in goat raising, while in the remaining instances in which other pursuits were followed raw goat's milk was used. In the case of the veterinarian, there was no use of goat's milk but he had worked with an infected goat placenta while having an unprotected wound on the hand. The bacteriologist was engaged in investigations with infected animals. In the abortus group there was a history of the use of raw cow's milk in twenty-one cases. Six were bacteriologists working with the organism, and two were laboratory workers who frequented abattoirs. The large number of infections among those working with the organism in the abortus series is probably due to the number so engaged in this country, for it is well appreciated that variety melitensis possesses a higher degree of virulence toward human beings, than does the abortus variety. It would seem, however, that melitensis infection was assuming the proportions of an industrial disease by reason of the large incidence of infection as a result of occupation. In many others there was a history of the use of milk from herds known to be infected. The degree to which the incidence of melitensis infection is confined to contact with goats is quite striking and bespeaks the natural limitations of the disease in this country. On the other hand abortus disease can in no way be so circumscribed.

Symptoms of onset. The symptoms of onset in both types of infection were quite varied, as one would expect. All degrees of severity of infection existed. Headache was much more prominent in the melitensis infections, occurring in 15, or 50 per cent, while it was present in 14, or only 26 per cent, of the abortus cases. General aching was, likewise, more prominent in the melitensis group, as was pain in the back of the neck, which occurred in 9, or 36 per cent of the former and in only 1, or 2 per cent, of the latter group. Fever occurred as a symptom of onset about equally in the two groups, in 16, or 64 per cent, of the melitensis cases and in 27, or 53 per cent, of the abortus cases. Chills and chilly sensations were, also, about equal in the two, being present in 16 per cent of the former and in 18 per cent of the latter. Other onset manifestations which occurred in the melitensis group were epigastric tenderness in two instances, and cramps in the legs, sore throat and neuralgia of the face in one each. Constipation was twice complained of at the onset. The abortus group showed a greater variety of less characteristic symptoms

of onset; fatigue occurring in eight, malaise in nine, sweats in eight, weakness in seven, joint pains in five, muscle pains in four, anorexia in five, aching in the legs in four, and nausea in four. Diarrhea and vomiting each occurred twice. Abdominal tenderness, backache, sore throat, precordial pain, dizziness, depression, insomnia and swelling of joints occurred in but one case each at the onset.

Sudden onset, when patients were acutely ill from the beginning, was more frequent in the melitensis group, while in only one case of abortus infection was the onset sudden. This was a laboratory infection in which headache, fever and chills were present as initial symptoms.

CLINICAL MANIFESTATIONS

The clinical picture in both types of infection varied to as great a degree as did the initial symptoms. The physical examination frequently showed nothing, while the most common abnormality was a palpable, and in some instances, tender spleen. The organ was felt in 12, or 48 per cent, of the melitensis group and in 16, or 32 per cent, of the abortus group. In several instances there was no mention of the spleen in the record, but a fact of probably some significance was its being reported as not felt in only 8 per cent of the former group, while such an observation was made in 44 per cent of the latter group. Evidences of pulmonary infection, bronchitis or râles at the bases of the lungs, were both infrequent and mild, and occurred in only one of the melitensis cases and in four of the abortus series. Epistaxis was encountered in three melitensis cases and in four of the abortus series. The objective joint manifestations were decidly more conspicuous in the melitensis group. Swollen and tender joints were found in 36 per cent of these cases, while they were present in only 11 per cent of the abortus group. Swelling of the knees was most frequently found during the course of the infection, occurring in 24 per cent of the melitensis cases and in 8 per cent of the abortus cases. In the latter group is included a case of intermittent hydrarthrosis, separately reported by Baker. In this case the organism was recovered from the joints, and the intermittent feature was so regular as to make the remission in one joint coincide exactly with the relapse in the other. Sweats occurred with about equal frequency, in 50 per cent of either series.

Subjective manifestations were, on the other hand, rather frequent. Of these gastro-intestinal symptoms were the most common, occurring in 84 per cent of the melitensis infections and in 70 per cent of the abortus infections. Constipation occupies the most prominent position and was seen in 64 per cent of the former and in only 10 per cent of the latter group. Tympanites was seen in 28 per cent of the melitensis cases while no mention was made of this symptom in the abortus group, and it was no doubt intimately associated with the constipation of the former. Abdominal tenderness and anorexia were about equal in the two series, but seen in only 10 per cent of the cases. Nausea and diarrhea were more frequently seen in abortus disease, occurring in about 12 per cent of the cases.

Joint symptoms were, likewise, much more prominent in the melitensis infections, present in 84 per cent of the cases, and in only 29 per cent of the abortus infections. Pain in the shoulders was decidedly more frequent in the former and also the most common joint symptom. It was present in 68 per cent of the melitensis series, while in only 6 per cent of the abortus cases. Pain in the back of the neck, pain in the knees and in the hips occurred in from 24 to 32 per cent of melitensis as compared with from 6 to 8 per cent of abortus cases.

Nervous manifestations were not definite in either series. Headache was the most frequent and was present in from half to two-thirds of both series. Other nervous symptoms mentioned were insomnia, neuralgic pains, neuritis, exaggerated reflexes, spasticity, dizziness, tremors, and depression, but none occurred in more than one or two instances.

Subjective respiratory symptoms were, as were the objective findings, very infrequent. Cough was present in 6 cases of either series, and pain in the chest was complained of in 3 melitensis and in 4 abortus cases.

Weakness was not a common symptom in either series. Loss of weight, which was dependent primarily upon the duration of the disease, was present in 7 of the melitensis series and in 13 of the abortus series. It is noteworthy that orchitis occurred in 5, or 20 per cent, of the melitensis cases and in 2, or 4 per cent, of the abortus cases. The recovery of the organism in pure culture from an ovarian cyst in a case of abortus disease, six years after the initial symptoms,

was a finding of particular interest. Blood stream infection was not present when the organism was recovered nor was there any evidence of a previously demonstrated agglutination reaction. Middle ear infections were found in 4 abortus cases, but these were all in children under four years of age. Manifestations occasionally seen were cramps in the legs, emaciation, pain over the spleen, blurred vision and weak eyesight, tonsillitis, and ethmoid infection. Eruptions, simulating rose spots, were present in two cases of abortus infection. Splenic infarction occurred in one case of abortus disease, and a cerebral accident in another, but a rheumatic endocarditis was present in both cases. In only a very few instances were the lymph nodes mentioned. In one case, an abortus infection, there was general lymph gland enlargement.

DURATION AND RELAPSES

In the recorded instances of the duration of illness in the melitensis group the infection lasted from one month to over one year. The average duration was 5.2 months, and the majority varied from two to ten months. In nine cases, however, there was no record of the duration.

In the abortus infections the duration of illness was from two weeks to two years. A large majority of the cases lasted less than six months. In 16 cases no record of the duration of illness was made.

The record as to relapses is quite incomplete as many of the cases were reported before the infection had actually terminated. In eight cases of melitensis infection there was no record. In one case there were eight relapses, in 4 several, in 2 three, in 2 one, and in 6 at least one. In 27 of the abortus series there was no record. In 1 case there were ten relapses, in 6 several, in 1 three, in 2 at least two, in 2 at least one and in 4 one. It is of some significance we feel, that there were no relapses in 9 cases of abortus diesase.

BLOOD AND URINE CULTURES

It is at once noted in Chart III that the percentage of cases in which there was no record of blood and urine cultures having been made was so large that the figures are of little value. However, it is noteworthy that the percentage of negative results in both urine and

blood cultures is appreciably higher in the abortus group, while the percentage of cases in which there is no record is fairly uniform. This may or may not be due to the difficulty usually experienced in obtaining an initial growth of the bovine strain of the abortus variety. In one case of melitensis infection a positive urine culture was obtained when the blood was negative. In one case of abortus infection, with a positive blood culture, no organisms were recovered from the urine but lesions were produced in a guinea pig when inoculated with the urine.

Blood. Observations on the blood of these cases also were too fragmentary to give any comparative figures. However, in 15, or

	POSITIVE		NEGATIVE		NO RECORD	
	Cases	Per cent	Cases	Per cent	Cases	Per cent
Blood culture:						
Melitensis	8	32	1	4	16	64
Abortus	14	27	16	32	19	42
Urine culture:						
Melitensis	5	20	1	4	19	76
Abortus	1	4	15	30	32	64

CHART III

more than half of the melitensis series, the record of "no anaemia" was made, while in five cases there was a record of "anaemia." In only three cases were estimations of the haemoglobin and red counts given. In two of these, the haemoglobin was 53 and 55 per cent, with red cell counts of 3.5 million, but we do not know the duration of illness at the time these observations were made. In the third case the haemoglobin was 75 per cent and the red cell count 4.25 million.

In the abortus group there are no records of observations in 20 cases, while in 6 the record of "normal blood" was made. In 11 cases the haemoglobin was over 80 per cent with corresponding red cell counts. In 8 cases the haemoglobin was below 80 per cent, ranging from 55 to 80 per cent, with red cell counts ranging from 3.0 million to 4.3 million. Here again we do not know at what time these observations were made.

In 18 cases of the melitensis group the white cell count is not

recorded, and in 22 no differential formula is given. In 7 cases the count is below 7000, ranging from 4000 to 7000. In one case there is a record of "moderate leucocytosis," and in another "no increase." In only 5 cases is the differential formula given, in four of which the P.M.N. count is recorded as less than 30 per cent in one case, from 40 to 50 per cent in one case, and from 50 to 60 per cent in three cases.

In the abortus group the white cell count is given in 35 cases. It ranges from 2000 to 3000 in 3 cases, from 3000 to 4000 in one case, from 4000 to 5000 in 10 cases, from 5000 to 6000 in 4 cases, from 7000 to 8000 in 8 cases, from 8000 to 10,000 in 4 cases, from 10,000 to 12,000 in 4 cases, and is over 12,000 in 2 cases. In two cases the record is "normal white cell count," and in another "leucopenia." In 28 cases the differential formula is given. In 16 cases no record is made, and in 6 it is recorded as normal. Of the 28 cases, in 6 the P.M.N. count is given as above 60 per cent, the highest being 78 per cent. In 21 instances it is below 60 per cent, of which 16 are below 50 per cent, 7 below 40 per cent, and 4 below 30 per cent. In one case it is recorded as "decreased." In 19 cases the lymphocyte count is above 30 per cent, in 16 above 40 per cent, in 7 above 50 per cent, and in 4 above 60 per cent, the highest being 76 per cent. In 14 cases the large mononuclear transitional count is given, the highest being 41 per cent. In 9 cases it was above 5 per cent, in 7 above 10 per cent, in 3 above 15 per cent and in one above 20 per cent.

Degree of agglutination reaction. In the melitensis series the titre of the sera ranged from 1–30 to 1–5280. These apparently represent the highest agglutination titre obtained, but we are unable to tell whether or not the reaction was present in all dilutions below those given. In 3 cases no titre is given, but it is, however, not recorded as absent. In one the blood yielded the organism, in the second it was present in the urine, and in the third case it was recovered post mortem from the spleen.

In the abortus series the titre ranged from 1–20 to 1–5120, and the same qualification concerning lower dilutions applies. In three cases, no titre is given, but it is not recorded as absent. In one case of our own series there was a definite proagglutinoid zone. In another, where an ovarian cyst yielded the organism in pure culture, the latter agglutinated in the serum of a different patient up to 1–640 with a

proagglutinoid zone from 1–20 to 1–160. The serum used had previously shown a proagglutinoid zone. At the time the organism was grown from the cyst no agglutination reaction could be obtained in the patient's serum, nor could it be developed by non-specific therapy (milk), although it was formerly present. No agglutination reaction was present in the serum in the case of intermittent hydrarthrosis at the time the organism was cultured from the joints, although it subsequently developed.

TYPE OF TEMPERATURE

In the melitensis group the temperature was undulant in 8, or 40 per cent, remittent in 6, or 24 per cent, and continued in 1, or 4 per cent. In the abortus series the temperature was undulant in 8, or 16 per cent, remittent in 23, or 46 per cent, and continued in 2, or 8 per cent. No record of the type of temperature was made in about one quarter of either series.

COMPARATIVE CONSIDERATIONS

1. The American incidence of melitensis infection is confined to the goat raising areas, while abortus infection is general and widespread.
2. The disease, presumably abortus infection, is much more prevalent than the literature would lead one to suspect.
3. Both infections occur in all age periods, but the occurrence of positive agglutinations in infants suggests the possibility that the disease is more common at this age than supposed.
4. The majority of infections of both types occur in males.
5. Occupation played a very important part in the melitensis infections. The incidence of contact infection from handling goats was so high that the disease assumed, in this small series, the proportions of an occupational disease. The high incidence of laboratory infection with the abortus variety entitles this organism, as well as the melitensis variety, to respect on the part of investigators.
6. Fever as a symptom of onset was by far the most constant. The severity of the symptoms of onset is certainly greater among the melitensis cases. The striking difference in the occurrence of pain in the back of the neck is worthy of note.

7. The physical examination was strikingly negative in both series, and little difference could be seen in the objective findings. Constipation was outstanding in the melitensis group, and there was frequently an associated tympanites. Joint pains and swellings of the joints were much more prominent in the melitensis cases, as was the occurrence of orchitis.

8. The occurrence of the abortus variety in an ovarian cyst six years after initial symptoms demonstrates the possibility of latent foci.

9. Records of absence of relapse was found only in the abortus group.

10. Normal or reduced white cell counts predominated in the series. There was a relative mononucleosis in a large percentage of the cases, but no striking variation could be found in the response in either group.

11. The existance of a proagglutinoid zone makes it imperative that all dilutions be made when the agglutination reaction is sought for, else the possibility of having missed the reaction in low dilution will always exist.

12. There is a possibility of the infection existing in the absence of the agglutination reaction in the serum.

13. The organism may be recovered from the blood and urine without demonstrable agglutinins in the serum.

14. The type of temperature is much more typical in the melitensis infections, although varied temperature curves occur.

15. The comparison of the two infections shows the melitensis infections to be generally more in accord with that described as Malta or Undulant Fever, and these infections are usually more severe than those caused by the abortus variety.

CASE REPORTS

Case 1. A. E., female, aged 47. History No. U-17884.

Family history. Unimportant.

Past history. Scarlet fever and measles in childhood. Influenza in 1918.

Present illness. Patient, a bacteriologist working with *Br. melitensis*, noticed in October, 1922, she was feeling bad. In March, 1923 found that she gave a positive agglutination for *Br. melitensis*, and in September the blood culture was positive. Was away from work for five months, then returned for seven months. She was again ill in July, 1924, and did not return to work until January, 1925.

A second relapse occurred in May, 1925, in which pain in the stomach before meals, relieved by eating, was a prominent symptom. On May 2nd there was a chill with fever. On May 4th physical examination showed nothing beyond a slight anemia. Liver and spleen were not palpable. Temperature continued slightly elevated during the month of May with constant afternoon rise. Beginning June 7 there was a remission until the 19th when the temperature again appeared and lasted until the 2nd of July. Temperature remained normal until the 16th when there was a relapse and on a few occasions would go as high as 101° in the afternoon. During the latter half of August there was another relapse. The remission following this was shorter and on the 29th fever again appeared, going as high as 101½°, and continued until September 20th. Fifth relapse occurred October 2nd and lasted until the 17th. This was followed by a remission which lasted until the 30th when a relapse again occurred, during which the fever went to 101½° and continued until November 18th. Fever was again present from November 30th to December 22nd. After a remission of six days, fever again appeared, lasting until the 16th of January. After six days of normal temperature the fever again rose in the afternoon to 100° and continued elevated until the 13th of February when a remission of three days occurred, followed by a relapse lasting until the 5th of March. During this period the patient received two transfusions and on May 6th, 1927, a blood examination showed a haemoglobin of 97 per cent, red count 4,000,000, white count 4,700. The differential count was 67½ per cent P.M.N., 2 per cent P.M.E., 27½ per cent lymphocytes, and mononuclears 3 per cent. Urine was negative except for a trace of albumin. Wassermann reaction was negative. Blood cultures were negative.

On July 18, 1927, melitensis vaccine was begun with varying reactions, at times urticaria, again malaise, pain in abdomen, and elevation of temperature. Its use was continued until September 12th. Beginning November 3rd she was given subcutaneous milk injections with some reaction after 2 cc. was reached. On December 5th vaccine therapy again used and continued until February 25th, 1928.

On April 14th, 1928, patient was admitted to Johns Hopkins Hospital, and on admission there was a normal temperature and a pulse rate of 78. Patient was a well developed, well nourished person, with no glandular enlargement. The heart and lungs were negative. Definite tenderness and muscle resistance was present in upper left quadrant. The spleen was not palpable. Blood examination—haemoglobin 90 per cent, red cells 4,600,000, white cells 6,500; P.M.N. 52.6 per cent, lymphocytes 42 per cent, mononuclears 4 per cent. Urine culture and blood culture were negative. No agglutination was obtained with *Br. melitensis*. Gastric contents were normal and stool negative. X-ray examinations of the stomach and intestines were negative except for some irregularity due to adhesions about the pylorus. Sinuses were clear and gall bladder visualizations negative.

On April 25th an irregular nodular mass the size of an orange was found in the cul-de-sac. It was tender but not indurated. On April 26th agglutinations with

Br. melitensis were again negative and for the third time on the 30th. There was at no time any elevation of the white count. On May 8th it was 7,500 and the same on May 10th. Repeated blood cultures were negative after at least two weeks incubation. On May 18th patient was given 20 cc. of convalescent Malta Fever serum, with a titre of 1–2600, without reaction. On the 21st the uterus and left ovary, which was cystic, and the left tube were removed. Cultures from the material contained in the cysts gave a pure culture of *Br. melitensis* which agglutinated 1–640 in a known abortus serum with a proagglutinoid zone from 1–20 to 1–160.

Case 2. J. F. G., female, aged 30.

Family history. Unimportant.

Past history. Irrelevant.

Present illness. Began January 28th, 1928 when patient developed fever with night sweats and later a sticking pain under left shoulder. Diagnosis of pleurisy was made. Temperature returned to normal in a few days but has been irregularly elevated since that time. Increasing weakness and feeling of exhaustion were the most prominent symptoms. Recently there has been some pain in upper left quadrant.

Physical examination, temperature 99.6°, pulse 96. Patient was undernourished, about twenty-five pounds. No evidence of any glandular enlargement. Heart and lungs were clear. Abdomen was somewhat enteroptotic. The liver was not palpable. There was resistance below the left costal margin and the spleen was palpable. Right kidney was also felt. Urine was negative. Blood examination: haemoglobin 80 per cent, red count 4,500,000, white count 6,400; P.M.N. 54 per cent, lymphocytes 39 per cent, large mononuclear transitions 7 per cent. Wassermann reaction on blood serum was negative. Blood culture yielded no growth.

Patient was admitted to hospital for further study. Nothing further found on physical examination. Five days after admission temperature went as high as 100° for five days. It then subsided and patient was free of fever until the 17th day when temperature elevation reached 102° upon one or two occasions and subsided by the 29th day. Spleen continued palpable, with intermittent pain in this region until shortly before discharge on May 27th.

Tuberculin reaction, 1–10,000 was negative. Widal gave a slight reaction in dilutions up to 1–100 with B. typhoid and Paratyphoid A. Three blood cultures and urine cultures were negative. On March 19th agglutination with *Br. melitensis* was negative but on the 29th it was positive 1–5,000, with no proagglutinoid zone. This was confirmed by the U. S. Public Health Service where agglutination with *Br. melitensis* 1–320 was obtained and with abortus, 1–160.

During the patient's stay in the hospital attempts were made to use a *Br. melitensis* vaccine, but sterile abscesses were regularly produced in spite of every effort to prevent them and the therapy was discontinued.

Patient was discharged much improved and since her discharge has been practically free of fever, but some pain has been intermittently present in the upper left quadrant.

Case 3. V. C. B., female, aged 32.

Complaint. Weakness and fever.

Family history. Unimportant.

Past history. Nothing of importance except that the patient was delicate up to the age of twenty years.

Present illness. In January 1924 patient was nervous with periods of depression and for a year was decidedly below par but nothing abnormal was found on examination. In February 1925 had a syncopal attack followed by an elevation of temperature to 102°. In March was thoroughly examined but nothing was found to explain condition. Patient continued to tire easily and found that she regularly had fever after exertion. In August a tooth was removed with some improvement.

Physical examination, September, 1925. Temperature 99.6°, pulse 96. Patient was well nourished and of healthy appearance and no abnormalities noted in the physical examination. Heart and lungs were clear, and liver and spleen not felt. Area of splenic dulness was not enlarged. Pelvic examination showed nothing abnormal. Blood examination: Haemoglobin 85 per cent, red count 4,700,000, white count 10,500; P.M.N. 78 per cent, lymphocytes 17 per cent, L. M. and T. 4 per cent.

Patient lived on a farm where the herd of cattle was infected with contagious abortion. The possibility of infection from this source was considered. Patient's blood serum was tested and found to give positive reactions in dilutions up to 1–160 with *Br. melitensis*.

Case 4. E. A., male, aged 32.

Complaint. Fever, cough and loss of weight.

Family history. Unimportant.

Past history. Irrelevant.

Present illness. Had an attack of grippe in February, 1926, with slow recovery, not well until May. Later had a return of constitutional symptoms, and on May 17 a chill followed by fever and sweat and tachycardia. There had been a slight cough present since February. Fever continued and in May patient was examined and was found to have a white count of 4,000. X-rays of chest were negative, but there was some clouding of the ethmoid cells. June 1st began to take quinine and fever disappeared to reappear in four days, and has continued elevated since that time. The white count was consistently subnormal and upon one occasion was 3,000 and upon another 2,000. There was a loss of twenty pounds in weight. On June 10th, 1926, physical examination showed temperature 99.6°, pulse 130. There was evidence of recent loss of weight, but some evidence of anemia. Heart and lungs were clear, and liver and spleen not palpable. Area of splenic dulness was not enlarged.

Patient admitted to the hospital where it was found that his haemoglobin was 92 per cent, red count 4,250,000, white count 3,400; P.M.N. 67 per cent, lymphocytes 32 per cent. Three subsequent blood examinations showed the white count ranging from 4,000 to 5,800, with P.M.N. percentage from 32 to 40 per cent and lymphocytes from 26 to 42 per cent. The large mononuclear transitional group varied from 22 to 41 per cent. Blood and urine cultures were negative. Wassermann reaction was negative. X-ray of chest showed lungs to be clear. There was no infection found in the urinary tract. There was evidence of chronic tonsillitis. Patient was discharged from the hospital unimproved.

In February, 1928, an agglutination of 1–80 with *Br. melitensis* was obtained with his serum. This was two years following the onset of his symptoms. There was an uneventful recovery.

Case 5. M. L. F., male, aged 47.

Family history. Unimportant.

Past history. Yellow fever in 1899. Four attacks of acute rheumatic fever, the last at the age of twenty. Had several malarial infections as a young man.

Present illness. January, 1927 two teeth were removed and recovery was slow. During February he did not feel well. There was easily induced fatigue and acute pain in the left hip, thought to be a bursitis. In March he experienced chilly sensations with a rise of temperature, and on March 20th had a frank chill with a temperature of 103°. At that time the physical examination was negative except for an acute coryza. X-ray examination showed some necrosis at site of tooth extraction. Socket was curetted and jaw healed without improvement in his general condition. Continued to run afternoon fever until April 15th when it reached 101°. During May fever was present but did not exceed 99.5°. Occasional digestive disturbances were present, but of no consequence.

Physical examination in May showed a well nourished, healthy appearing man. Temperature 99.4°, pulse 84. Operative scar on the upper right jaw. There was glandular enlargement. Heart and lungs were normal. Liver and spleen were not felt and splenic dulness was not increased. There was no evidence of infection in the urinary tract nor any evidence of infection in the nose and throat. Teeth were entirely clear of infection and nothing abnormal found in the gastro-intestinal tract. Urine was negative except for a trace of sugar on two occasions, and a trace of albumin and a few pus cells in the sediment. Gastric contents and stool were normal. Blood sugar—121 mgm. There was an agglutination with Paratyphoid B up to 1–80. Blood cultures were repeatedly negative. From March until May 5th five blood examinations were made, with haemoglobin estimations above 90 per cent and red cell counts above 4,700,000. White count varied from 4,000 to 7,400. The P.M.N. percentage varied from 27 to 64 per cent and the lymphocyte percentage from 29 to 60 per cent. The large mononuclear-transitional cell percentage was within normal limits throughout. On May 19th there was agglutination with *Br. melitensis* 1–1280 and on June 3rd 1–2060.

Case 6. W. E. M., male, aged 21.

Complaint. Headache, stomach trouble, and vomiting.

Family history. Negative.

Past history. Unimportant except for scarlet fever at ten and influenza in 1918.

Present illness. Began October 20, 1924 with headache, loss of weight and weakness, followed by griping abdominal pains, nausea and vomiting, which had no relation to meals. Abdominal pain continued and in four days became intermittent. There was some blurring of vision. No joint tenderness was present. Tendency to constipation developed. There were no chills but constant elevation of temperature.

Physical examination, November 3, 1924—temperature 102°, pulse 96. Heart and lungs were clear. Abdomen was negative except that the spleen was definitely palpable. Extremities were negative. Blood examination showed 5,300,000 red cells, white count 13,500, haemoglobin 92 per cent, P.M.N. 61 per cent, lymphocytes 31 per cent, L. M. and T. 7 per cent. Widal reaction was negative. Urine culture was negative. Wassermann reaction was negative. Six blood cultures were negative. Three urine cultures were negative. On November 13th there was agglutination with *Br. melitensis* 1–1280 and on the 13th 1–5120. The white count continued above 10,000. During the patient's stay in the hospital temperature continued to reach 101° and 102° in the evening and gradually subsided. Was discharged much improved.

Case 7. This is the case reported by Keefer in the Johns Hopkins Hospital Bulletin, vol. 35, page 6, 1924.

Case 8. This case will be reported by Baker in Archives of Internal Medicine.

Note. Since these cases were collected, three additional cases have come to our attention, which were not included in the series. They all occurred in Maryland.

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OPERATIONS ON THE THYROID GLAND[1, 2]

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There is in the Museum of the Detroit Medical College, contributed by a distinguished surgeon of Western Michigan, a pathological specimen of the trachea and thyroid gland of a child who had died of suffocation consequent upon thyroidal enlargement. Another instance of death from the same cause is reported to have occurred within a few years in the city of Detroit. Probably neither of these deaths would have taken place, had the attending physicians not been deterred from operating by the exaggerated accounts, which are copied into all the textbooks, of the extreme danger of operative procedures on this organ. Whatever may be the perils of such operations when undertaken for the removal of old goitres, or the large bronchoceles of Graves' disease, there can be no question that the profession have

[1] Reprinted from the Detroit Clinic, vol. 1, no. 1, p. 1, January 4, 1882.

[2] EDITORIAL NOTE: The paper by Dr. Theodore A. McGraw on "Operations on the Thyroid Gland" was first published in the "Detroit Clinic" in 1882, a periodical which survived only one year. In 1918 Dr. Halsted endeavored to obtain the volume in which the paper appeared, but was unable to find it in the Surgeon-General's Library. Search by Dr. R. D. McClure in Detroit, at the time, failed to bring to light the volume of the defunct periodical, and the search had to be abandoned. Dr. Halsted's interest in the article was due to the belief that Dr. McGraw's paper was the first report in America of a complete removal of a thyroid gland. He was trying to obtain the paper for his own contribution on "The Operative Treatment of Goitre." Recently the volume in which the article appeared was found in the Detroit Public Library, and Dr. McClure had it copied and kindly submitted it to the BULLETIN. It has seemed to the Editors that the paper should be reprinted because of its possible historical significance, and also that a brief biographical note of the author might well accompany the article.

According to an account by Professor Frederick A. Coller of the University of Michigan, published in the *Journal of the Michigan State Medical Society* in January, 1929, Dr. McGraw was born in Detroit in 1839 and received the Bachelor of Arts degree from the University of Michigan in 1859. He began the study of

greatly erred in supposing that these dangers were common to *all* operations on the thyroid gland. While my own experience in such operations is small, it is nevertheless large enough to convince me that the risks of incising or removing the thyroid body are not greater than those which attend similar procedures on other tumors of the neck which have attained equal size.

My first operation of this kind was on the person of Mrs. X., a colored woman who entered the college clinic with a cyst as large as a hen's egg in the right half of the thyroid gland. It was not only unsightly but also threatening in character, as it caused occasional severe breathing. I cut down upon it, separated it easily from the surrounding tissues, tied the right superior and inferior vessels and cut through the isthmus, removing one-half of the gland. There was almost no hemorrhage, and excepting for a slight keloidal development in the scar, recovery was rapid and complete.

In the winter of 1879, a French girl of twenty entered St. Mary's Hospital with a cyst as large as a walnut in the thyroidal isthmus. I incised it, removed its anterior wall and destroyed its base with carbolic acid. No bleeding point required a ligature, and healing by granulation took place in two weeks' time.

The next case was Mrs. N., living near Washington, Macomb County, Michigan. This patient, thirty-seven years of age, consulted me in June, 1880, about a cystic enlargement of the whole thyroid gland. The principal, central, tumor was surrounded by numerous

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medicine in Germany, and obtained the degree of Doctor of Medicine from the College of Physicians and Surgeons in New York in 1863. Immediately after receiving his medical degree, he became a contract surgeon in the United States Army, and served in that capacity throughout the remaining years of the Civil War. He was, at one time in charge of a surgical ward in a military hospital in Chattanooga, and later, while attached to the staff of General J. H. Wilson, and in charge of wounded soldiers left behind by the Union Army, was captured by Confederate forces operating under General Forrest. After the war he was one of those instrumental in founding the Detroit College of Medicine where he occupied the chair of Surgery. Later, when the school was reorganized, he became president and dean. He seems always to have taken a lively interest in medical education, and to have been a frequent contributor to medical journals. That he enjoyed the profound respect and admiration of his colleagues and pupils can scarcely be doubted by those who have read Professor Coller's article.

smaller cysts. It had been growing for two years, had reached the size of an orange, and had of late caused a difficulty in breathing which at times was quite serious. On July 12, assisted by Drs. Yates of Washington, Chamberlin of Romeo, and Boice of Detroit, I removed the entire gland. There was almost no hemorrhage, though fourteen ligatures were left in the wound. The patient was a feeble woman, but recovered, nevertheless, without a bad symptom.

Finally, I operated on Christian M., of Detroit, a boy of fourteen years, for the removal of a bilobular cystic tumor of the thyroid gland of many years' growth. I had tried in vain to destroy it by electrolysis, and it continued to grow in size until it interfered seriously with his breathing. When I operated on March 7, 1881, the tumor projected like two base balls on both sides of his neck. There were present Drs. Kiefer, Reynolds, Henderson, Cleland and Boice. The dissection was tedious, but otherwise without serious difficulties. The bleeding was not at all profuse. Thirty-one ligatures were left in the wound. The operation was performed under the carbolic spray, and was dressed antiseptically. He recovered as rapidly as could have been expected after an operation of that magnitude. Total loss of voice followed the operation, probably from some injury done to the laryngeal, not from incision, for it was not exposed, but probably from traction. This patient has regained his strength but slowly. His voice has returned, but is feeble. His face seems somewhat bloated, and he complains of lack of strength and some rheumatic soreness of the muscles. The wound healed in about four weeks, but now, after seven months he seems dull and listless and indisposed to exertion. I am unable to discover any organic disease, and have faith that time will bring full recovery.

The operation for the removal of the thyroid gland is not very difficult, nor, in my opinion, excessively dangerous. If the surgeon, indeed, proceeds in its conduct as did the late William Warren Greene, he may expect terrific hemorrhage, and bring his patient to the very gates of death. The thyroid gland is very vascular, and is connected with the surrounding connective tissue, by numerous fragile blood vessels. If these are broken they will bleed furiously. Now, the secret of removing the thyroid gland without loss of blood is to proceed with great deliberation and caution, and tie every blood vessel, even

the smallest, between two ligatures, before either cutting or breaking it. This method of procedure is neither brilliant nor rapid, but it is eminently safe. The thirty-one ligatures left in the wound in my last case corresponded to the thirty-one left on the tumor when removed. Sixty-two ligatures made a tedious operation, but the patient lost almost no blood.

I would not be misunderstood as regards the dangers of thyroidal incision. The removal of the tumors in Metzer's neck left an immense wound, extending deep into the neck on both sides of the trachea, and exposing most important structures. Such operations must always be dangerous. This I feel warranted in saying: that the danger will be in most cases in direct proportion to the size of the tumor, other things being equal, and that it will not be greater than in operations for tumors of the same size and situation, but of different anatomical character. In every case the dangers of the operation must be balanced against those of the disease and the surgeon must act accordingly.

CHRONIC NEPHRITIS FOLLOWING ECLAMPSIA

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It has long been known that following eclampsia a woman may in a subsequent pregnancy have a second similar attack, or show evidences of chronic nephritis. The probability of either occurring has, however, been considered extremely small. Thus, Olshausen in 1892 found only two recurrences following 200 cases of eclampsia. Lepage quotes Charpentier as stating that women having eclampsia in one pregnancy are immune during others. Lepage found that in 22 primiparae with eclampsia there was no recurrence in subsequent pregnancies, but two out of 11 multiparae suffered a second attack. Bumm states in his textbook that 10 per cent of eclamptic women have a second attack, while Williams believes that a woman who has had eclampsia is less likely to suffer an attack in future pregnancies than one who has never had it. Hinselmann in a comprehensive review of available statistics found recurrences in 1.92 per cent.

On the other hand, one often obtains a history of a previous toxemia of pregnancy in a patient with chronic nephritis. Post and Stieglitz, on inquiring into the antecedents of a series of nephritic women, found that 50 per cent of their patients under the age of 45 presented a history of preceding toxemia of pregnancy. Several authors have found a few of their eclamptic patients returning with a definite nephritis. Slemons in 1913 in a series of 20 eclamptic women noted 1 patient who in the following pregnancy had a severe toxemia, probably nephritic. Harris studied 27 women a year after an eclamptic attack and found definite evidences of chronic nephritis in three. Döderlein, Jr., in a similar study of 26 post-eclamptic patients found that 16 were normal, 7 with urine containing albumin and casts, 3 normal except for slight albuminuria, and 1 with hypertension. He believes that true nephritis after eclampsia is rare, and that when it exists he is inclined to believe that it has antedated the eclampsia. Greenhill traced 60 patients after eclampsia; two died of nephritis two and three and one-half years later, and three of those living had definite

chronic nephritis. He believed that four of these 5 patients were nephritics at the time of their convulsive attack. Nevermann examined a similar series of 60 patients; 27 were normal, 30 had some of the following symptoms—headache, weakness of memory, visual disturbances, oedema, hypertension, cloudy urine, or albumin and casts, and 3 had frank severe chronic nephritis. Thirty-six of the above were seen in subsequent pregnancies, 2 had questionable nephropathies and 4 a second eclamptic attack.

In 1919, it became the policy in this Clinic to attempt to have all patients return for reëxamination thirteen months after delivery, particular efforts being made by our Social Service workers to insure the return of all toxemic patients, as well as others of exceptional interest. During the past few months, we have reëxamined as many as possible of the patients who have had eclampsia since this time. In this way, it has been possible to obtain data on 74 patients representing 77 attacks of eclampsia; (3 patients having had a second attack on the service). In the 9 years ending December 31, 1927, 128 cases of eclampsia were observed on the service, so that this study comprises 60.2 per cent of the total number of cases which came under observation.

These patients were particularly studied to determine the presence or absence of chronic nephritis. Symptoms such as headache, backache, visual disturbances, oedema, and nycturia were especially noted. The blood pressure was determined and the urine examined for albumin and casts. Ophthalmological studies were done on most of them. Some, whose condition after these determinations was in doubt, were admitted to the hospital for further study. Of the entire number, a surprisingly large percentage were found to present definite evidences of chronic nephritis. In the following analysis, only those patients in whom the diagnosis seemed beyond criticism are included in the nephritic group. Several others with slight hypertension, a trace of albumin in the urine, or presenting indefinite symptoms have been set down as normal.

The following is an analysis of the results obtained from the examination of post-eclamptic patients a year after delivery in an effort to ascertain whether any features of the convulsive attack may predispose the patient to the development of a subsequent nephritis.

As stated above, 74 post-eclamptic women have been examined, 3

having had a second attack on the service, making a total of 77 cases of eclampsia. One year later, 17 of these patients were found to have chronic nephritis, an incidence of 23.0 per cent of the patients, or 22.1 per cent of the cases of eclampsia.

The patients were first divided into the mild or severe types of eclampsia, according to Eden's classification, when it was found that 38 were in the former and 39 in the latter category. Five mild cases returned with nephritis (13.2 per cent), as compared to 12 (30.8 per cent) in the severe group. Dividing the cases according to the time of onset of the eclamptic attack, we found 38 with antepartum, 24 with intrapartum, and 15 with postpartum eclampsia. Twelve of the antepartum cases fell in the nephritic group, or 31.6 per cent. Of these, 13 patients presented intercurrent eclampsia, delivered forty-eight hours or more following cessation of the convulsive attack, and 2 of these (15.4 per cent) returned with nephritis. In the 24 cases of intrapartum eclampsia there were 3 nephritics (12.5 per cent) as compared with 2 (13.5 per cent) in the 15 postpartum cases.

Grouping the series according to both of the above classifications, we obtain the following data.

TYPE	MILD ECLAMPSIA			SEVERE ECLAMPSIA		
	Cases	Nephritis	Per cent	Cases	Nephritis	Per cent
Antepartum	17	5	29.4	21	7	33.3
Intercurrent	8	0	00.0	5	2	40.0
Intrapartum	13	0	00.0	11	3	27.3
Postpartum	8	0	00.0	7	2	28.6

It will be noted that all of the mild cases returning with nephritis fall in the antepartum group, while in the severe eclampsias all types seem about equally subject to a succeeding nephropathy.

The age and parity of the patients at the time of the eclamptic attack were next studied, as shown in the accompanying table:

AGE	CASES	NEPHRITIS	PER CENT
To 19 (inc.)	34	4	11.8
20–29	29	4	13.8
30–39	11	7	63.6
40 and over	3	2	66.6

Thus it would seem that the older the woman at the time of eclampsia, the more liable she is to a resultant nephritis. Forty-nine of the patients were primiparae, and 28 multiparae; 12.2 per cent of the former and 39.3 per cent of the latter subsequently showed signs of nephritis. Consequently, age and multiparity both seem to act as predisposing factors in the development of permanently diseased kidneys.

An inquiry into the previous history of the patients was then made; 5 had had a previous toxemia with convulsions, 3 on the service and 2 elsewhere, and 3 of them were found to have nephritis a year after the second attack. It is interesting to note that the 3 patients whose first eclampsia was observed by us had showed no evidence of renal involvement after the initial attack but developed it after the second one. Two other patients had been seen by us previously with a non-convulsive toxemia, and both of them were normal a year after the eclamptic attack. The remaining 67 patients gave no history suggesting previous toxemia, nor did careful questioning give any indication of impaired renal function prior to the eclampsia. If any of these women had a kidney lesion before delivery it was certainly not sufficient to have given rise to any discomfort.

The time of onset of convulsions varied from the sixth month of pregnancy to forty-eight hours post partum. Forty-three of the women were at term, and of these 5, or 11.6 per cent, developed nephritis. Of the 34 before term, 12 or 35.3 per cent showed involvement at the end of the year.

The duration of symptoms prior to the actual convulsive attack was investigated. The patient was questioned as to headache, oedema, visual disturbances, backache, and epigastric pain. In those women receiving prenatal care at the Clinic, the time of first appearance of hypertension or albuminuria was determined. In 23 of our patients no signs or symptoms indicating preëclampsia could be elicited, many of these falling in the postpartum eclamptic group; yet 2 of them (8.7 per cent), were later nephritic. The remaining 54 had had symptoms or signs for a period of time varying from a few hours to over a month. Our investigations apparently show that the actual length of time during which symptoms were present, or in other words, during which one might expect tissue damage to be taking

place, made no difference so far as a subsequent nephritis was concerned. Actually less nephritis was noted in patients presenting symptoms for two weeks or more than in those under one week. However, 15 cases of nephritis developed in the women who had some symptoms prior to the attack, a percentage of 27.8; three times as great as in the asymptomatic cases.

It was thought that the number of convulsions might be of significance, in that a patient with eclampsia severe enough to give rise to many convulsions would seem more likely to sustain permanent kidney damage. Thirty-seven of our patients had less than 6 fits, while in 5 there were over 20, the upper limit being 32. On grouping our cases after this fashion, it was found that the number of convulsions had no effect at all, since as large a percentage of nephritis was found in patients with few as with many seizures.

The duration of the convulsive attack varied considerably. Eleven of the patients had only one fit. In the remaining the duration varied, with an upper limit of seven days from the first to last convulsion. Very little difference was noted in the number of nephritics grouped in this way, though there was a percentage incidence of 15.8 nephritis when the attack lasted under six hours as against one of 28.2 when the duration was longer.

The degree of hypertension at the time of eclampsia was now studied, with rather significant results.

SYSTOLIC PRESSURE	CASES	NEPHRITIS	PER CENT
mm.			
To 170	24	0	00.0
171–200	26	4	15.4
201 and above	27	13	48.1

The table shows that in no patient with a systolic blood pressure of 170 mm. or less did nephritis develop, while in about half of those with hypertension over 200 mm. there was evidence of permanent renal damage. An analysis of the diastolic pressure gave similar results. In 23 patients this was 110 mm. or below, and none of these became nephritic. In 41 the pressure varied from 111 to 130 mm. and 9 of these (21.9 per cent) later had nephritis. In 12 cases with a

pressure of over 130, 8 (66.7 per cent) showed chronic renal damage. Similar findings were noted when the pulse pressure was considered, and 9 of the nephritic women fell into a group of 22 patients who presented a pulse pressure of over 80 (40.9 per cent).

Albuminuria, as measured in grams per liter by the Esbach method, showed that the frequency of nephritis corresponded approximately to the amount of albumin.

ALBUMINURIA	CASES	NEPHRITIS	PER CENT
grams			
To 1	13	0	00.0
1.1–5	23	3	13.0
5.1–10	22	6	27.3
10.1 and over	18	8	44.4
?	1	0	00.0

The above chart indicates that the greater the albuminuria the greater becomes the probability of an ensuing nephritis. There were 10 patients with a blood pressure of 170 mm. or less and albuminuria of not more than 1 gram. Some of these were, clinically, extremely ill and two of them had 23 and 18 convulsions respectively; yet in none of them did nephritis develop. On the other hand, there were 10 cases with a hypertension of 200 mm. or above and with 10 or more grams of albumin per liter of urine. Only one of these patients had more than 9 convulsions, and in general they did not appear to be seriously ill. In 6 the hypertension and albuminuria cleared up reasonably promptly and they left the hospital apparently normal; nevertheless, when they returned at the end of a year, 8 out of the above 10 had definite chronic nephritis.

We have also studied the effect of coma, tachycardia, and hyperpyrexia during the eclamptic attack. No connection between the first two conditions and a subsequent nephritis could be made out; but in the patients presenting fever, which we have learned to regard as an ominous sign, the percentage incidence of nephritis fairly closely follows the extent of increase of body temperature.

No connection whatever could be found between abnormal findings in the chemistry of the blood during the eclamptic attack and an ensuing nephritis. Analysis of the figures of blood non-protein

nitrogen showed that a high reading giving indication of nitrogenous retention was not evidence that the patient had or would develop nephritis. Six patients had a non-protein nitrogen reading of over 50 mgm. per 100 cc., the highest being 85 mgm. All of these were quite normal at the end of a year. A high blood uric acid, reaching in 1 case to 12.3 mgm. per 100 cc. also afforded no indication; nor could any correlation be established between nephritis and hyperglycemia, such as was seen in many cases. The same was true on analysis of readings for the carbon dioxide combining power of the blood.

It was thought that the length of time elapsing between the onset of the convulsive attack and delivery, in other words, the duration of profound toxemia during which permanent tissue damage could develop, might prove significant. Such proved not to be the case, as the lowest percentage incidence of nephritis was noted in the 11 cases in whom delivery was not effected until three days or more after the onset of actual eclampsia.

A study of the course of labor and delivery of the patients was made. The duration of labor varied from that noted in 3 patients on whom Caesarean section was practiced prior to the onset of pains, to over forty-eight hours. Neither the length of labor nor its severity had anything to do with a resultant nephritis. Likewise, the type of delivery, whether spontaneous or operative, made no difference. It might be stated that except for 6 patients, three delivered by Caesarean section and three by *accouchement forcé*, all deliveries were by conservative procedures, the other operations consisting of induction of labor by bougie or bag, and forceps during the second stage. The anaesthetic chosen at the time of operation or delivery was also without significance, and 8 cases of nephritis were found in the 31 patients who at no time had received any general anaesthetic.

We now come to the study of the course of hypertension and albuminuria during the puerperium. Our eclamptic patients remain in the hospital under observation for a minimum of three weeks, and longer if there is any abnormality at that time. In 75 per cent of the patients the blood pressure fell to normal within fifteen days after delivery, yet 13 of them returned with nephritis at the end of a year. On the other hand, only 4 of the 11 patients who were discharged with

some hypertension showed a nephritis later. Albumin disappeared from the urine relatively much more slowly than the hypertension fell, and in less than 60 per cent of the patients was the urine albumin free at the end of fifteen days. Seventeen patients were discharged from the hospital with more than a trace of albumin in the urine, yet only 3 of these had nephritis later. On the other hand, 14 women developed nephritis who were albumin-free three weeks after the eclamptic attack.

Thirteen of the patients were examined for hypertension and albuminuria six weeks post partum, and only 4 were found to be normal, yet at the end of a year 1 of these 4 had nephritis. Of the 9 patients who at this time had persistent high blood pressure and urinary albumin, 4 cleared up later and were normal when again seen. Accordingly, it would seem that we are not only wrong in attempting to establish a final diagnosis three weeks post partum, but even at six weeks we cannot be sure whether or not the patient is normal or has permanent kidney damage.

Of the 74 patients in the series, 25 have since been delivered on the service, and only 11 of them went through a normal pregnancy and delivery. As has been stated, 3 had a second eclamptic attack; 6 showed a definite nephritic toxemia, of whom 3 required therapeutic abortion and sterilization. Four patients had a mild toxemia, diagnosed as low reserve kidney, and 1 a premature separation of the placenta. In this series at least, the favorable prognosis ordinarily given the eclamptic woman for subsequent pregnancies does not seem to be borne out.

Finally, it seemed of interest to investigate the question of prenatal care of the patients in our series. We do not consider that a patient has received adequate prenatal care unless she has paid at least 3 dispensary visits, giving a minimum period of six weeks of observation prior to delivery. Examinations are made every four weeks up to the seventh month and at intervals of two weeks thereafter. Fifty-one of the patients had never been seen by us prior to the eclamptic attack; 5 others had been registered on the service but had made less than 3 dispensary visits, so that their care was considered inadequate. There remain 21 patients who were under our care for six weeks or longer prior to the eclampsia, yet in spite of reasonable prenatal care, ulti-

mately developed this very serious disease and in 4 of these nephritis was evident later. Six of these patients had a normal course throughout in the dispensary and were seen within two weeks of the eclamptic attack. One patient was normal throughout in the dispensary but was not seen within two weeks of the eclampsia. We do not feel that these cases of eclampsia were due in any way to neglect on our part. Four other patients were normal in the antenatal clinic until their last visit, when toxemic signs were found and they were admitted to the hospital. In these cases the eclampsia developed after admission. However, the remaining 10 patients showed signs of toxemia in one or more visits to the dispensary. One was advised admission but refused, while the other 9 were treated at home under dietary therapy and close observation. They were all considered mild toxemias, with slight hypertension and albuminuria and few symptoms. Yet eclampsia developed in all of these. This experience illustrates very well our inability in some cases to distinguish between a mild toxemia and one which will eventuate in eclampsia, and shows the fallacy of considering any toxemia as innocuous until after delivery. We feel that under ideal circumstances every toxemic patient should be hospitalized, and regardless of her subsequent course should remain under observation until after delivery. Unfortunately, this is usually impossible both from the financial and social status of the majority of our patients, which does not permit their remaining long away from their households. Moreover, crowded ward conditions as well as the expense to the hospital from a prolonged stay, makes such an ideal almost unattainable.

Of the above 21 patients, 4 developed fits at home; 6 were admitted with preëclampsia, and developed convulsions within twelve hours of admission and before any therapy might have a chance to act. Eleven patients, however, developed convulsions after being on the service for twelve or more hours. Such unfortunate occurrences must happen until we have some method of accurately gauging the severity of preëclampsia. Fortunately, none of this last mentioned group showed a later renal involvement, although 4 cases of nephritis developed in the remaining 10 patients who visited the dispensary for the prescribed number of times.

DISCUSSION

In this series of 77 cases, a relatively large percentage, 22.1, were found at the end of a year following an eclamptic attack, to have a definite chronic nephritis. Whether or not the nephritis antedated the eclampsia, and the cases really represented "eclampsia superimposed upon chronic nephritis," cannot be said. However, the lack of such indications in the previous history and the physical well-being of these women prior to the toxemia speak against it. Also, we cannot say that the nephritis did not develop entirely independently after the subsidence of the eclampsia. This again seems unlikely from the history and course of the patients concerned. Certainly it seems possible that a disease of the severity of eclampsia and one which at the autopsy table in the majority of cases shows definite renal lesions sometimes might be expected to leave the patient who recovers with permanently impaired kidneys.

From this point of view, it would be expected that more nephritis would be found in the severe than in the mild eclampsias, and such is the case,—as we noted a percentage incidence over twice as high following the former. Likewise, the high incidence of nephritis in antepartum as compared with intrapartum and postpartum eclampsia seems rather explicable. We found no cases of nephritis in mild intra- and postpartum eclampsia, but in all the types of severe cases some chronic nephritis developed. The age of the patient seemed to be definitely correlated; whereas only 4 cases of nephritis were found in the 34 women having eclampsia below the age of 20, there were 9 such in the 14 who were over 30 years old. A similar observation is made from the point of view of parity, since relatively three times as much nephritis followed in multiparous as in primiparous women. The patient developing eclampsia before reaching term seems more liable to nephritis later. Likewise, those in whom eclampsia develops without preceding symptoms are better off at the end of the year than those in whom the attack is ushered in by a period of premonitory symptoms. The number of convulsions during the eclampsia does not appear to have any bearing on this problem. Relatively, the number of nephritics seen after an attack of eclampsia with 5 or less convulsions was no greater than when the patient had 20 or more. Likewise, the duration of the convulsive attack seemed to play little

part, though on grouping the cases according to whether the attack lasted for less than six hours, or longer, we find relatively more predisposition toward nephritis on the side of the longer duration.

On the contrary, there seems to be a definite relation between the degrees of hypertension and the amount of albuminuria, as the incidence of nephritis increased definitely with the elevation of blood pressure and the number of grams per liter of urinary albumin. Thus, with a systolic blood pressure under 170 and 1 gram or less of albumin, we did not find a single case of nephritis; whereas, with a pressure of 200 or more, and an albumin content of at least 10 grams, 8 of 10 cases fell into the nephritic group. Moreover, our findings indicate that high diastolic and pulse pressure readings have the same significance.

No connection can be adduced between abnormal findings in the chemistry of the blood and a later nephritis. In none of our patients with a definitely elevated blood non-protein nitrogen did nephritis develop. Likewise, the time elapsing between the first convulsion and delivery, as well as the actual duration of labor, the type of delivery, or the kind of anaesthetic used, seem to play no particular part in the development of chronic nephritis.

The rate of return to normal of the blood pressure is of some significance. Thirteen cases of nephritis were found in those women discharged from the hospital three weeks post partum with a normal blood pressure. There was a higher percentage incidence of nephritis when the patient was discharged with hypertension, yet in 7 of 11 such cases the pressure later fell to its usual figure and a year later the patient was normal. Albumin in the urine cleared up relatively more slowly than the hypertension. Seventeen patients were discharged at the end of three weeks with more than a trace of albumin, yet in all but 3 the kidneys were apparently quite in the *status quo ante* at the end of a year. Even six weeks post partum was not long enough to make a definite diagnosis. Four of 9 patients who had both hypertension and albuminuria at this time later cleared up and were normal.

The prognosis for subsequent pregnancies following an eclampsia seems gloomy. In only 11 out of 25 such cases in this series was the whole course without incident. Three patients had a second eclampsia, 6 a nephritis, and 4 a mild toxemia, diagnosed low reserve kidney.

If this is generally true, it would seem advisable for us to view more seriously the outcome for the child in eclampsia.

The greater portion of our patients had received no prenatal care, only 21 women having attended the dispensary for 3 or more visits, though these women should have had quite adequate care as they received 6.9 visits per person. Yet eclampsia developed. In several patients the outbreak came within two weeks of an examination, at which time there was no hypertension or albuminuria and no alarming symptoms. Other patients were admitted as soon as an abnormality was noted, yet developed convulsions prior to delivery. Ten patients were seen one or more times in the dispensary, with definite though relatively mild findings indicative of toxemia and were treated at home. These women either developed convulsions at home or were later admitted with grave symptoms and thereafter developed eclampsia. Eleven patients developed eclampsia more than twelve hours after admission to the Clinic. This affords still further illustration of our profound ignorance of the cause of eclampsia and hence its treatment. Even adequate prenatal care will not do away entirely with the disease. With our present knowledge it seems better to err on the side of pessimism and regard all cases of late toxemia of pregnancy as potential eclampsia until after delivery.

CONCLUSIONS

1. A surprisingly large percentage of eclamptic women are found to have definite though relatively mild chronic nephritis a year or more after the attack.

2. Much more nephritis follows severe than mild eclampsia, and it is more likely to develop after the antepartum type. The latter is particularly true when the eclampsia develops at some time before the pregnancy has reached term.

3. The percentage incidence of nephritis increases with the age of the patient, and multiparous women are more prone to it than primiparous.

4. Out of 5 cases of repeated eclampsia, nephritis developed in 3 after the second attack. None of these patients gave a history indicative of chronic kidney disease prior to the convulsive attack.

5. There appears to be no connection between the number of con-

vulsions and subsequent nephritis. However, it develops relatively less frequently when the duration of the convulsive attack is under six hours.

6. There seems to be a direct relation between the amount of hypertension and albuminuria and later permanently impaired kidneys. With a pressure of 200 or more and albuminuria of at least 10 grams, three-quarters of the patients ultimately develop nephritis.

7. The blood chemistry at the time of eclampsia gives no indication of what may develop later.

8. Neither the duration from onset of eclampsia to delivery, the length or type of labor, nor the type of anaesthetic employed at delivery can be correlated with a later nephritis.

9. A slow return of blood pressure to normal is suggestive. However, nephritis may develop within the year, even in patients who were discharged with a normal pressure and negative urine. On the other hand, hypertension and albuminuria persisting throughout the puerperium do not necessarily indicate that the kidneys will sustain permanent damage.

10. The outlook for a subsequent pregnancy following eclampsia is less favorable than is generally believed.

11. Even the most adequate prenatal care will not always prevent eclampsia. Consequently, all toxemias should be carefully watched since even the mildest types may occasionally eventuate in an altogether unexpected eclamptic attack.

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BOOK REVIEWS

Childbirth. By WILLIAM GEORGE LEE, A.B., M.D. 300 pp. $3.00. (*University of Chicago Press, Chicago, 1928.*)

In the introduction to this book Dr. David S. Hillis says, "Out of a large experience as a clinician and teacher of obstetrics the author presents his subject in a simple form as well adapted to the needs of the beginner as to those of the mature student of the obstetric art. Indeed, a layman with sufficient interest in the subject would find most of the book within his grasp."

This statement, although meant as a laudatory one, shows clearly why the book misses fire. No book can be of scientific value to laymen, students of medicine and specialists alike.

The author has written an outline of obstetrics in words of one syllable, so to speak. He talks of the child as "babe," the umbilical cord as "navel string," the membranes as "bag of waters." In fact, every scientific term is explained by two or three very simple synonyms.

Important accepted obstetrical facts are entirely omitted from this work. Generalizations are made which seem much too dogmatic and even rather naïve; for example "Sepsis almost never occurs when a competent obstetrician is in charge" and again " . . . . childbed fever is responsible today for many deaths despite the fact that for more than fifty years absolute knowledge has been present of how to avoid it."

Numerous debatable points of technic and procedure are advocated by the author. The book, on the whole, is a very superficial and inadequate discussion of the subject.

B. L. M.

Diseases of the Nose, Throat and Ear. Edited by A. Logan Turner. Second edition, revised and enlarged. 440 pp. $6.00. (*William Wood and Company, New York, 1927.*)

In the preface it is stated that the book is to be kept within the reasonable compass primarily suitable for the senior student and the practitioner of medicine. With this as an avowed purpose it would have been better to approach the subject with emphasis upon the relation of otolaryngological disorders to general medical conditions, and with a particular effort to inform the senior student and the general practitioner just what he might expect from an otolaryngological consultation. It does not seem appropriate in such a book to enter into great detail concerning surgical operations. This is stepping beyond the "reasonable compass." The descriptions are necessarily limited and consequently in many instances they are incomplete. This space could have been devoted more profitably to a discussion

of the indications for operations and an evaluation of the end results in the experience of the authors.

On the whole, there is a very agreeable correlation between the anatomical, the physiological and the clinical aspects. For example, the clinical significance of the variation of the anatomy of the sinuses is most satisfactorily discussed. It is rather noteworthy that in the description of the technique of the examination of the nasopharynx no mention is made of the use of the electric nasopharyngoscope. In America it is regarded as one of our most important instruments.

It is interesting to note that almost one half of the book is devoted to diseases of the ear. The internal ear receives much more detailed attention than one finds in the average text-book and the consideration includes all of the important recent contributions. The discussion of otosclerosis is particularly good. In this portion of the book, also, much space is given to surgical operations. Even the operations for labyrinthitis are considered in great detail. In America these procedures have been practically abandoned.

The book includes all of the important material for a proper treatise on the diseases of the nose, throat and ear. This material is well assembled and more fully reviewed than in the average text-book.

M. L. B.

Surgical Diagnosis in Tabular Outline for Students and Physicians. By DR. A. J. CEMACH. Authorized translation, with additions and notes. By Edward L. Bortz, M.D. With an introductory note, by John B. Deaver, M.D. $12.00. (*F. A. Davis Company, Philadelphia, 1928.*)

This volume represents a vast amount of work in the assembling of much useful information. It is as free from faults, so far as form and substance are concerned, as any similar work could be. While very useful in the hands of the busy surgeon and teacher, it will probably do harm in the hands of undergraduate students, if used alone, by robbing them of the gripping interest derived from a slow, but continuous approach to the heart of the subject as supplied by most modern text books.

The book will probably find a relatively large field of usefulness in the office of surgeons, but it will not be as effectual as a similar scheme worked out by each surgeon for his own use.

It will be valuable as an adjuvant when used with one of the modern systems of surgery.

E. H. H.

Child Health and Character. By ELIZABETH M. SLOAN CHESSER, M.D. 204 pp. $1.50. (*Oxford University Press, New York, 1927.*)

The author of this little book of 200 pages has dealt with all the difficulties, physical and psychological, of the modern nursery. Pre-natal advice to the mother, the care and training of the child from infancy through adolescence are

set forth in a presentation both pleasantly readable and easily comprehensible to the non-medical reader. The chief value of the work lies in the formulation of groups of definite rules—sane and sensible and worthy of being used as a working basis by mother, nurse, or other child supervisor. The elaboration and explanation of these rules is less satisfactory. In trying to simplify such a large and varied field, the writer tends to become superficial and inaccurate in her statements. One is left with the impression that the final solution of all behavior difficulties is biochemistry. Future generations may find this to be true, but our present state of scientific knowledge concerning behavior certainly gives no indication that biochemistry has discovered the key to human nature. It is not only unwise but misleading to tell parent and teacher that "an alert vital child" may be richer in thyroid secretion than a more "stupid morose brother;" or that "cowardice is often a matter of gland deficiency. Deficiency of pituitary secretion produces a moral and intellectual inferiority, whilst the adrenal glands situated on top of the kidneys are called the glands of combat, because of their influence on fight, flight, and fear. Those who are rich in adrenal secretion are not fearful but pugnacious."

The author lays great stress upon the physical care of the child, finding in it frequently the solution of mental traits: laziness for example, may be due to the toxin from decayed teeth. "Remove the septic teeth and the character alters." In the two chapters devoted to the adolescent the emphasis is entirely on the physical needs, and one is left with the feeling that good physical health and good mental health, as expressed by "good character" are synonymous; that if the adolescent is in good physical condition he will easily adjust to the mental and emotional strains put upon him.

Much of the advice is especially suited to the British public, and is of passing interest only to others. Most American mothers would find it as difficult to argue with the author on the subject of poor boarding-school cooking and woolen clothing, as the American medical man would find it difficult to argue with her on the etiology of chorea.

E. L. R.

Treatment of Venereal Diseases in General Practice. By E. T. BURKE, D.S.O., M.B., Ch.B. (Glas.). 162 pp. $1.75. (*Oxford University Press, New York, 1927.*)

The reviewer believes that there is no excuse for the publication of this book in the United States and but little for its appearance in England. The author's aim is to write a small manual of treatment of venereal disease for the use of the general practitioner. In his introduction he bewails the lethargy of British chemical manufacturers as compared with the enterprise of those in other countries and says, "There are a great many foreign preparations on the market for the treatment of syphilis; and here one would most strongly emphasize the fact that there should be no necessity to go abroad for such drugs." Throughout the text of the book he lives up to this statement and advises the use of many proprietary drugs, the

names and composition of which are certainly unfamiliar to those outside Great Britain, and the value of most of which is unsupported by any evidence known to the reviewer. For example, he advises the use of Stabilarsan (a glucose arsphenamine, Sulfarsenol (these are the only two arsphenamine products recommended), Bismostab (metallic bismuth in glucose), colloidal bismuth cream for inunctions, intramine, contramine, sanitas, and in case the usual iodides are not tolerated by the patient, a series of proprietary compounds including iodicin, iodoglycine, riodine, tiodine, collosol iodine, iodargol, iodex ointment and, for inunctions, iodolysin and iodinosol. There is certainly not the slightest evidence that inunctions of iodine products, no matter how carried out, are effective. Even Kolynos tooth paste is mentioned. For the treatment of acute anterior gonorrhea he recommends detoxicated vaccines, the intramuscular injection of S. U. P. 36 and S. U. M. 36, and for gonorrhea in women, spuman.

These lists suffice to indicate the character of the book which seems more of an advertisement for unnamed British pharmaceutical houses than a scientific effort. The text is filled with such mis-statements of fact as "exfoliative dermatitis [following arsphenamine] . . . . is most prone to occur [among other conditions] in those suffering from pyorrhea alveolaris." There are many more important issues on which the author would find few competent syphilologists to agree with him, as for example when he says "One might express the relative value of the antisyphilitic triad as follows: arsenic 10, bismuth 8, mercury 3," and the statement that mercury "is as obsolete as sarsaparilla."

The book adds one more to the author's pungent statement in his introduction: "The shelves of the medical bookshops groan under a load of colorless tomes on venereal disease."

J. E. M.

The Holy Incense. A Botanical, Pharmacological, Psychological and Archaeological Appreciation of the Bible. By DAVID I. MACHT, A.B., M.D., LL.B., Phar.D. 81 pp. (*Williams & Wilkins Company, Baltimore, 1928.*)

In the present volume Doctor Macht devotes himself to the task of discussing the Biblical Incense not only from the traditional archaeological and ritualistic standpoint, but in addition from the aspect of modern natural sciences such as botany, chemistry and pharmacology. The problem could not have found a more competent treatment than in the hands of the author who is well known as a successful investigator in the field of pharmacology, but also masters all the tools indispensable for an authoritative presentation of the historical and archaeological sides of the problem.

An exhaustive discussion is given of the four principle constituents of the Holy Incense mentioned in the Bible itself, stacte, galbanum, frankincense and onycha, and the various adjuvant ingredients handed down by the oral law. The interest of the medical reader will be particularly attracted by the chapters dealing with the pharmacological properties of incense and their bearing on the psychology

of the ancient Hebrew rites. On the basis of experimental investigations Doctor Macht calls attention to the antiseptic and bactericidal activity of the essential oils volatilized in the fumes of incense and points out the possible hygienic significance of this fact in connection with its still widespread use in the Orient.

In the discussion the writer clearly indicates his deep and fervid appreciation of the Bible as embracing in its higher wisdom, though empirically, the justification of the use of the Holy Incense as viewed from the modern standpoint.

O. W.

Erythema Nodosum. By J. Odery Symes, M.D. 73 pp. $2.00. (*William Wood and Company, New York, 1928.*)

This is a very interesting and instructive little monograph of 70 pages, giving the experiences of the author with a relatively large number of cases of erythema nodosum, which have apparently been closely and intelligently observed and followed. He has emphasized and brought out clearly the general symptoms preceding the eruptive stage of the disease and shows in table form the differential diagnostic points between it and acute rheumatic fever. He was unable, in the study of 3 cases, to substantiate the theory that the disease is due to the local action of bacteria. The pathological report was that it is an acute arteriolitis, suggesting some soluble toxin as the cause. The author believes that the affection is not related to erythema multiforme but that there is some association between it and tuberculosis which, however, is the exception rather than the rule.

The book is well worth perusing by either the dermatologist or internist.

L. W. K.

A Text-Book of Pharmacology and Therapeutics. By Hugh Alister McQuigan, Professor of Pharmacology and Therapeutics, University of Illinois. 660 pp. $6.00. (*W. B. Saunders Co., Philadelphia, 1928.*)

The book before us, like most textbooks, can be discussed from two points of view. It may be evaluated in comparison with other standard texts on the subject, or it may be weighed on its own merits. Compared with the outstanding original works by Cushny, Sollmann, and Dixon, or English translations of Poulsson and Meyer and Gottlieb, or even with the more empirical Pharmacotherapeutics of Solis-Cohen and Githens, the present work does not fill a vital gap. It is at most only a faithful exposition of the author's conception of pharmacology which can easily be discerned to be the work of a Ph.D. in chemistry who has shifted into medicine. This explains the emphasis placed on subjects primarily of biochemical interest, such as proteins, lipins, and what the author calls "proximate principles," the profusion of chemical formulae, the disquisitions on hydrogen, oxygen, nitrogen, etc.

Considered on its own merits, the present textbook possesses many excellent, but not uniformly excellent, features. In many respects it is surprisingly up-to-date, as, for instance, in giving the chemistry of sterols. Digitalis covers eighteen

pages. There is a very good discussion of antiseptics covering fifty pages and the book, unlike many other textbooks, gives fair space to antipyretics of the coal-tar series and also contains an instructive chapter on local anesthetics. The treatment of laxatives is excellent and supplemented with striking illustrations and colored plates. Wise judgment is exhibited in devoting adequate space to radioactive substances, which are bound to play an important rôle in the medicine of the future. On the other hand, many of the articles are notably poor. For instance, epinephrin and ephedrin are given but too little space. The description of ergot is inadequate. Opium, perhaps the most important of all drugs, is dealt with in an extremely superficial manner.

The classification employed is rather puzzling and one cannot well make out its rationale. Another deplorable feature is the extremely meager bibliography and the few literary references cited are surprising in the antitheses which they present. Thus, under pituitary principles, the two references quoted are the paper by Abel in the Johns Hopkins Hospital Bulletin, 1924, Vol. 35, page 305, and that by Kamm and his collaborators in the Journal of the American Chemical Society, 1928, Vol. 50, page 573. Again, the all important subject of digitalis is dismissed with two literary references, one being by A. R. Cushny and the other by G. Canby Robinson! Elsewhere, the court of highest and only authority to be cited seems to be the Council on Pharmacy and Chemistry of the American Medical Association. A minor, but highly laudable, feature of the work is a philological one, namely, brief references to the etymology of the various pharmacological terms employed.

D. I. M.

Practical Clinical Laboratory Diagnosis. A Thoroughly Illustrated Laboratory Guide Including the Interpretation of Laboratory Findings. By CHARLES C. BASS, M.D., and FOSTER M. JOHNS, M.D. Third edition, completely revised. 187 pp. $7.50. (*The Williams & Wilkins Company, Baltimore, 1929.*)

This volume should be useful to those who propose to conduct their own clinical laboratory examinations. It is full of practical hints based upon wide experience. It is, of course, a laboratory guide only, and not a text-book. It is profusely illustrated, perhaps too much so, for the illustrations have made it necessary for a book containing 187 pages to sell for $7.50. One wonders whether it is necessary to publish illustrations of microscopes taken from instrument makers' catalogues. It seems to the reviewer that it is unfair to the purchaser of the book to make him pay for the cost of illustrations that, after all, do not add very much to our knowledge or technique. There are one or two omissions in the text which deserve remark. One misses a description of the method of preparing blood smears with cover-slips rather than slides, and one misses, also, a description of the appearance of fresh preparations of blood. On the whole, the book is satisfactory for the purpose it is supposed to serve, but it seems unnecessarily expensive.

A. M. C.

A Short History of Medicine. By CHARLES SINGER, M.A., M.D., D.Litt. Oxford. 368 pp. $3.00. (*Oxford University Press, New York, 1928.*)

There are few medical historians better qualified than the author of this work for the task of writing a short book, for students and non-medical readers. It is no mean task and as the author states no two writers would choose the same examples or allot the same amount of space to each subject. Dr. Singer's work is fittingly inscribed to Dr. E. T. Withington who has himself written one of the most fascinating short accounts of the history of medicine extant.

The book is divided into six parts; the first five take just half the volume and the author sketches rapidly but skillfully the medicine of ancient Greece and the Alexandrian School and Roman medicine which grew from Greek roots. Naturally these two sections center largely around Hippocrates and Galen. The middle ages with the Arabians and some accounts of medieval hospitals and hygiene are considered in the third part and the rebirth of science, Vesalius and the awakening of anatomy and the transition from alchemy to chemistry take up the fourth section.

The period from about 1700 to about 1825 Singer styles "The Period of Consolidation." In this we have the development of science, its application to medicine and the rise of clinical teaching. The last half of the book takes in the modern period which the author calls "The Period of Scientific Subdivision." Here we have succinct accounts of preventive medicine, physiology, experimental medicine, surgery, bacteriology, psychology, nursing, the action of drugs and the interpretation of collective medical data.

The choice of material is excellent. To pick out the salient features of these subjects and dispose of them satisfactorily in a few words is a difficult task as only one who has tried it can realize, but Singer had has an unusual preparation for such a study and his work shows it. If there is any fault it is that more space is accorded non-medical science than such a short work would warrant even when such science is closely bound up with the history of medicine. Perhaps the English physicians and scientists come in for a little more prominence than they would be accorded by a French, Italian or German historian, but that is to be expected.

This book may be recommended not only for the student and layman for whom it was written but for the physician who has neglected the history of the development of his profession. It will awaken an interest in the trends of medicine and prepare the reader for the fascinating study of the sources from which the material was derived.

J. R.

Spinal Anesthesia. By CHARLES H. EVANS, M.D. Introduction by W. Wayne Babcock, M.D., F.A.C.S. Foreword by Charles Gordon Heyd, M.D., F.A.C.S. 203 pp. $5.50. (*Paul B. Hoeber, Inc., New York, 1929.*)

During the past several years the increasing number of publications on spinal anesthesia has given evidence of its spreading popularity. Only within the past

few months one of the prominent surgical journals devoted an entire number to the subject. It is fortunate for users of spinal anesthesia that we are thus able to compare different opinions regarding controversial points and so approach more closely the best utilization of an early ideal method of anesthesia. Dr. Evans has written a very complete résumé of the subject up to the present time. His experience has been gained as Clinical Assistant in the New York Post-Graduate Medical School and Hospital, the Lying-In Hospital of the City of New York and as Surgeon in the (Orange) New Jersey Orthopedic Hospital. His book gives in orderly detail his own experience, and his opinions on such debated questions as the choice of anesthetic agents, the use of adrenalin and ephedrine as stimulants, and the position of the patient during anesthesia. There is much more to spinal anesthesia than the simple injection of novocain in the subarachnoid space and Dr. Evans gives much valuable information on the preparation of the patient for anesthesia, the care of the patient during anesthesia and the avoidance of complications. His book is timely and useful.

E. M. H.

Epilepsy. By WILLIAM G. LENNOX and STANLEY COBB. Medicine Monographs, vol. 8. 197 pp. $3.50. (*Williams and Wilkins, Baltimore, 1928.*)

It is not possible to summarize the contents of this book, since it is itself a condensation of a very large material. The scientific literature on epileptic convulsion states is carefully collected and concisely summarized. The authors maintain throughout an open-minded and at the same time critical attitude. The result is an excellent survey of our present day knowledge of the subject. Investigative and practical therapeutic aspects are given equal weight.

After reading this book one cannot help being struck with the meagreness of our actual knowledge of the etiology of epileptic convulsions. "We are forced," as the authors say, "to postulate some unknown constitutional element." It is one of the chief merits of the authors that they map out so clearly the directions in which further progress of scientific study may be expected.

Every physician who is interested in the subject of epilepsy, from either the therapeutic or from the investigative angle, will find this very clearly written and lucidly organized book indispensable as a guide to a very difficult subject.

F. I. W.

Textbook of Clinical Neurology. For Students and Practitioners. By M. NEUSTAEDTER, M.D., Ph.D. With an Introduction by Edward D. Fisher, M.D. 602 pp. $6.00. (*F. A. Davis Company, Philadelphia, 1929.*)

This book possesses no qualities which could recommend it and many for which it could be condemned. The author's style lacks clarity. In a vain effort at succinctness words vital to comprehension are frequently omitted, e.g., the opening sentence of the paragraph on the etiology and pathology of tics, "As a defense reaction, involving a relatively small group of muscles, it is purely mental." There are frequent solecisms at which even the non-meticulous must cavil; e.g., the

heading, "Brain Hemorrhage," the phrases "No pathology was found," "Endocarditis and post-operative hemiplegias mean embolism," and in speaking of Wilson's disease, "The most apparent and characteristic symptom is Parkinson's syndrome associated with liver cirrhosis." A note of didacticism which the reviewer considers unsound is constantly struck. The words "always," "never," "invariably" appear in nearly every paragraph. There is no bibliography whatever.

The author's own subjects of research, the use of horse serum in the treatment of poliomyelitis and the diagnosis of neurological conditions by "tremograms" are given undue value. The anatomy and physiology of the nervous system are given very scant attention.

There are a great many observations and opinions with which the reviewer disagrees, the presence of a typical tremor in dementia praecox, the prohibition of spiced foods for the arteriopathic, the value of the relative degree of papilloedema as a sign for localizing the side on which a posterior fossa tumor lies, the grouping of migraine with the trophoneuroses, the irritative hypophyseal tumors are responsible for adiposogenital distrophy, the value of fractional doses of calomel in the treatment of encephalitis, that autointoxication plays a prominent rôle in the production of Jacksonian fits in infantile hemiplegics, that the mentality of defective infantile hemiplegics "may in the course of time return to normal," the value of a purin-free diet in chorea and epilepsy, that all recovered cases of acute meningitis have "permanent defects," that a sudden cessation of menstruation can produce hematomyelia, that there is always ptosis of the lids in myasthenia gravis, that in myasthenia gravis "the accumulation of toxic products in the circulation acts as an exciting cause on points of minor resistance congenitally acquired," that the electrical reactions of hysterics are pathological, that cantharides plaster is of value in Bell's palsy, that "to-day we know that both (rheumatic fever and chorea) are due to an infection by a specific streptococcus," that dystonia musculorum "may appear as a sequel of Wilson's disease," that "vasomotor, secretory and trophic disturbances are always associated with tics," that the pathology of tic doloureux is that of neuritis," that "children with a neuropathic taint cannot undertake professional careers," the advisability of "firm pressure upon the gonads" to stop functional convulsions, that to distinguish a traumatic neurosis from a case of malingering one should "rely solely upon objective findings, irrespective of the subjective complaints and the history of trauma." Among these objective findings are listed spastic pupils to light and accommodation, with hippus, abnormal amounts of urates and creatinin in the blood and urine, and alimentary glycosuria.

The absence of any mention of the use of iodine therapy in the treatment of Graves' disease, the acidotic diet in epilepsy, and the Freudian concepts in the discussion of hysteria are striking in a textbook copyrighted in 1929. This book offers an unfortunate contrast to Wechsler's splendid "Textbook of Clinical Neurology" published two years ago.

M. S. G.

The Heart in Modern Practice. Diagnosis and Treatment. By WILLIAM DUNCAN REID, A.B., M.D. Second edition revised and enlarged. 466 pp. (*J. B. Lippincott Company, Philadelphia and London, 1928.*)

The author of this book has an apparent desire to present the subject of heart disease to the practising physician in such a way that it may be grasped without too much effort and understood without especial training in the technique of cardiology. The result is a very sound, simple and readable volume.

Angina pectoris and coronary disease are viewed in this book as separate entities. For example, on page 21 is the statement: "the diagnosis (of angina) is made by a study of the symptoms and not from the data obtained by other methods of examination." On page 360 the author states "Alteration in the ventricular complex in the electrocardiogram may be observed in coronary infarction but not in angina pectoris; in the latter abnormal findings, if present, are those of the heart disease with which the anginal syndrome is associated." The theory of angina pectoris, as set forth, is that this condition is a clinical syndrome brought on by a failure of the peripheral vascular bed to respond by dilatation on exercise; this failure of vascular accommodation in turn causes an increase in pressure at the root of the aorta and in the heart.

In other words, the author, in common with other writers upon this subject, believes that angina pectoris is a syndrome that is only accidentally related to heart disease and that it is possible to differentiate angina from coronary disease. If it were true that angina were only a matter of pressure relations, we should expect the worse prognosis in the case of permanent marked hypertension. Yet just the reverse is true: it is a commonplace of practice that the outlook is most grave for the patient with angina and normal blood pressure. The characteristic anginal syndrome occurring with certain cases of mitral stenosis, for example, in young people can not be explained readily on the basis of the writer's theory, if we understand it correctly. The reviewer feels that the attempt of some modern writers to draw a sharp line of division between the clinical syndrome of angina and heart disease is doomed to failure. Meanwhile, the practising physician is making daily use of the electrocardiogram which, when positive, serves as an aid in the differentiation of angina from gall-stones, spondylitis, hysteria and a host of other conditions.

We believe that statistical study will fail to support the author's statement that pure atheroma rarely causes aortic insufficiency, though many experienced clinicians hold the same opinion: there is need of more light on the subject from combined clinical and pathological studies.

On page 99 the murmur of mitral stenosis is described as occurring "immediately following the second sound." This is not in accord with common clinical observation that this murmur follows the second sound by an appreciable interval and is usually initiated by a third heart sound, or "opening click" of mitral stenosis.

The strength of the book lies in its judicious correlation of technical and bedside data, its common sense, and its careful presentation of valuable information con-

cerning treatment of various cardiac conditions. The laws relating to the production of cardiac murmurs are unusually well presented. It is a good book on the whole subject of heart disease in practice and has the advantage in this sense over those volumes devoted only to the physical signs, or the arrhythmias, or to any one aspect of this large subject.

If much of this review has concerned itself with apparent criticism of the book in question, it was occasioned merely by the desire to point out other aspects of the angina problem. Such comment should not be considered to detract from the fundamental excellence of the author's book which is almost unique in American literature and which will prove highly valuable to many readers.

J. T. K.

Handbook of Microscopical Technique. For workers in both animal and plant tissues. Edited by C. E. McClung, Ph.D. Illustrated. 495 pp. $8.00. (*Paul B. Hoeber, Inc., New York, 1929.*)

The present volume consists of eleven chapters written by twenty-five contributors, including the editor, Professor McClung. The book is divided into a chapter on General Methods and into ten chapters on Special Methods, the latter section comprising: II. Methods for the Study of Fresh Material, III. Bacteriological method, IV. General Botanical Methods, V. Cytological Methods, VI. Embryological Methods, VII. Histological Methods, VIII. Protozoological Methods, IX. Fixation and Fixatives, X. Stains and Staining, XI. Miscellaneous.

The methods for the study of fresh material indicate the modern trend of investigations in cytology and histology and are new to a book of this kind. There are sections on microdissection and microinjection by Chambers, on vital stains by Foot, and on supravital staining by Sabin, covering in all some fifty pages. Under histological methods, it is stimulating to find sections by different individuals upon such diversified subjects as methods of studying red blood cells, methods for the study of leucocytes, histological technique for the study of bone, dental histological technique, methods for the intercellular substance of the connective tissues, methods for preparing muscle and electric organ tissues, neurological technique including that for neuroglia and microglia (the metallic methods).

This work has the disadvantages of any compilation made by a group of contributors. There is a certain amount of reduplication and there are obivous omissions. As examples of the latter, the absence of any specific references to histological investigation of the internal ear and the organ of Corti, or of the retina, might be mentioned. On the other hand, the work has advantages which more than counterbalance its defects. It presents personal experience and exercises critical judgment in a way which it is impossible for only one or several authors to do. The citation of a great amount of unsatisfactory and useless material is eliminated by the collaboration of a number of authors each presenting his own field. As a result, it is not left to the investigator, consulting the book, to discover laboriously whether the methods quoted are either antiquated or impracticable. Because of the saving in space by the elimination of unnecessary

methods, it has been possible to widen the scope of the volume, to include such interesting and valuable topics as the methods for the study of fresh material and embryological methods.

On the whole the volume is to be highly recommended. The print and paper are excellent. The material is well arranged with respect to chapter headings and subheadings and the index is adequate. The price of the book is $8.00.

G. B. W.

Collected Papers of the Mayo Clinic and the Mayo Foundation. Edited by Mrs. M. H. Mellish and H. Burton Logie, M.D. Volume 19. 1330 pp. ~~$3.00~~. (*W. B. Saunders Company, Philadelphia, 1928.*) #13.00

A wealth of material is available at the source from which these papers have been collected. Out of a total of 398 papers collected for the year 1927 one hundred are reproduced in full, thirty-four abridged, forty-four abstracted and 220 are referred to by title.

The papers are grouped under the following headings: alimentary tract, urogenital organs, ductless glands, blood and circulatory organs, skin and syphilis, head, trunk and extremities, chest, brain, spinal cord, nerves, and miscellaneous. The general and special fields of medicine and surgery are included in each group, and papers of interest to the greatest number are reproduced in full with ample illustrations, charts, tables and bibliographies. This volume should be a very desirable asset to the general surgeon and diagnostician.

W. I. N.

The Toxemias of Pregnancy. By H. J. STANDER. Medicine Monograph, XV. xi + 161 pp. $3.00. (*The Williams & Wilkins Company, Baltimore, 1929.*)

This monograph presents a very thorough review of our present knowledge of the etiology, symptomatology, metabolism, and treatment of the toxemias of pregnancy. The main topics treated are: changes in normal pregnancy, vomiting, low reserve kidney conditions, nephritis, pre-eclampsia, eclampsia, and acute yellow atrophy of the liver. More than half of the monograph is rightly allotted to a discussion of eclampsia. While the sections dealing with the chemical and metabolic changes are particularly comprehensive and authoritative, the aspects of etiology and especially the discussion of the prevailing methods of treatment are sufficiently extensive and well correlated. A bibliography of approximately 800 references renders this otherwise valuable monograph all the more useful to the student of this subject.

W. A. P.

Partnerships, Combinations and Antagonisms in Disease. By EDWARD C. B. IBOTSON, M.D. 348 pages $3.50. (*F. A. Davis Company, Philadelphia, 1929.*)

The title of the book is quite alluring. There is today a keen interest in the biology of disease, the effect of one disease upon another and the possible rôle of

antagonistic ones in therapeutics. The use of the malaria parasite in the treatment of syphilis of the central nervous system did much to reawaken this line of thought although there is no agreement as to whether this is an instance of true antagonism between the malaria parasite and the treponema or merely a therapeutic effect of an abrupt high elevation of body temperature.

The book is nicely illustrated with portraits of a number of eminent physicians whose works have been milestones in the progress of medicine—men like Bright, Pierre-Marie, Addison and Osler.

In the preface the author states that the object of the book is to encourage others to produce a better one so that in the long run the "subject may bear fruit."

The first quarter of the book is devoted to the influence of heredity in disease, and exposition of the importance of the individual constitution, constitutional types or diatheses.

The next fourth considers the relation of tuberculosis to other diseases and constitutional diatheses. Then a number of other infectious diseases are considered such as leprosy, syphilis and smallpox with particular attention to their effect on the susceptibility of the individual to other diseases or the degree to which they themselves are influenced by other morbid conditions.

Next there is a section on physiology in which the interrelation of the larger organs of the body such as the heart and lungs, skin and kidney is discussed in a general sort of way.

Finally the rôle of the endocrine glands and the influence of the nervous system on disease is considered.

The scope of the book is very attractive. The text, however, impresses the reviewer as of little value either to the medical student or as a reference book, although quite interesting reading in places. It is a rather loosely woven collection of items of all sorts—case histories, statistical summaries, therapeutic suggestions, theories of disease behavior, endocrinology, etc.—gathered from medical literature and now and then from the author's personal experience. There is little or no attempt at critical evaluation of the works quoted so that unless the reader himself is already sufficiently trained to form his own valuations correctly, he may take them all as of equal value. Too often statements of opinion are made as if they were accepted doctrine. The book will sell on its title but many readers will undoubtedly be disappointed in its contents.

A. C. S.

Blood and Urine Chemistry. By R. B. H. Gradwohl and Ida E. Gradwohl. 542 pp. $10.00. (*The C. V. Mosby Company, St. Louis, 1928.*)

This large pretentious looking volume proves on closer examination of its contents a sad disappointment. Its bulk is made up chiefly by almost life-size illustrations, taken from catalogues, of such familiar objects as test-tubes, beakers, flasks, etc. The descriptions of the methods are given in the form of cookbook directions. References to the original articles in which the methods were elabo-

rated are not cited. They are quite evidently intended for rather ignorant "technicians" devoid of chemical training.

It is the rise in late years of a relatively large class of such "technicians" which is responsible for the mass of uncritical chemical data which obstruct our literature. It is not true that anybody who can read the simple English of chemical analytical manuals can perform the really complicated and precise analyses. The reviewer firmly believes, furthermore, that abbreviated, chopped up, step by step "notes" on any given analytical method can never take the place of a careful study of the author's own description of the genesis and development of the method, of his comparative data, of his statement of the pitfalls and of necessary precautions, of the limits of accuracy and applicability of the proposed procedure. But all of this and the ability to assimilate it presupposes at least a modicum of chemical training on the part of the analyst, a factor with which the authors of this manual are evidently not concerned. Otherwise it is difficult to see any reason for this book. It presents no valuable addition to the already available and infinitely superior American texts on this subject, from which, indeed, the authors have borrowed freely many tables, paragraphs, and illustrations.

This manual is furthermore remarkably incomplete and inadequate when its size is considered. Thus the newer and the widely accepted methods for blood sugar of both Folin and Benedict are omitted. No accurate methods are given for hemoglobin estimation, nor for the blood gases.

The second part of the book dealing with the clinical interpretations of the chemical data again consists of very long and diffuse verbatim quotations from the literature, which for the most part are neither very relevant nor instructive. The price for the book is high beyond reason.

W. A. P.